# Palifornia MEDICINE

OFFICIAL JOURNAL OF THE CALIFORNIA MEDICAL ASSOCIATION
© 1947, by the California Medical Association

vol. 66

APRIL, 1947

NO. 4

## Public Relations of a State Medical Society\*

JOHN W. CLINE, M.D., San Francisco
President-Elect of the California Medical Association

T is difficult to find an adequate definition of "Public Relations." When applied to any segment of society, the term obviously refers to the estimate of the public concerning that particular group. If that opinion be good, the group may be said to enjoy "good public relations" and if the opinion be poor, the converse is true. The terms "good" and "bad" are relative and not absolute. It follows, therefore, that things can be done which may result in the improvement or deterioration of the relationship of a particular group to the public.

There is little or no difficulty in presenting the scientific achievements of medicine to the people. News sources are avid for this information. The tendency is for writers in lay publications to dramatize and exaggerate such news beyond its proper value.

The function of the medical profession in our society is to provide adequate medical care of high standard within the economic reach of the bulk of our people. The profession, itself, must be the judge of the standard and adequacy of care. No other group is equipped with the knowledge and experience to determine these points. One frequently encounters efforts on the part of laymen to set down rules and regulations concerning these items. The theoretical and emotional background of these opinions is apparent and sometimes would be amusing, were it not for the serious consequences involved.

It is probable, however, that the public will have a considerable influence upon the decision as to what constitutes adequacy of medical care.

The situation is somewhat different when it comes to the determination of what constitutes provision of such care within the economic capacity of the public. Here the people have a right to participate in the decision and, whether we wish it or not, probably will have the ultimately dominant voice.

It is apparent that public opinion will be a vital factor in shaping the future pattern of medical care and the method of its distribution. It is, therefore, necessary that the public be well informed so that its attitude toward medicine and medical care will be intelligent and based upon fact instead of emotion and prejudice.

This is the basis upon which any effective public relations program must be built. We must further realize that the technical field of public relations is one with which the medical profession is not familiar. We should seek the advice and services of experts in this endeavor, just as our patients come to us for medical care.

About three years ago, the Council of the California Medical Association belatedly reached this conclusion. Earlier, abortive efforts had been made in this direction and the experience had not been pleasant. It was evident that we needed the advice of someone who possessed recognized abilities in this sphere.

We, therefore, sought the advice of one of the largest and best known advertising agencies in the country. The approach of this organization to our problem was remarkably similar to that which we utilize in solving the medical problems of our patients. In both fields effective therapy depends upon accurate diagnosis. In this instance, the diagnostic procedure consisted of a public opinion survey. This was conducted according to standard methods and was designed to ascertain the attitude of the public toward the medical profession and the individual physician.

The survey showed that the public held a rather high opinion of its doctors as individuals and felt

<sup>\*</sup> Delivered by invitation before the Mid-Winter Clinical Sessions of the Colorado Medical Society, Denver, February 19, 1947.

that they did a good job. The estimate of the profession as a whole was not as high. The principal complaint was against the costs of medical care. There was an expressed desire for prepaid medical care and the preference was for voluntary rather than compulsory insurance.

A correlated survey of the attitude of the physicians of the State showed that there was very little enthusiasm for, and in some instances open opposition to California Physicians' Service, our own plan for prepaid medical care. It was also demonstrated that the individual physician had very little knowledge of the problems confronting his profession.

We have found it extremely difficult to keep the average physician adequately informed. In many instances he does not read his state journal or at least that part which has to do with medical association activities and the general welfare of the profession. He is more inclined to read a short, concise bulletin, particularly if it has glaring headlines. He can be reached through hospital staff meetings more easily than in any other way.

#### PHYSICIANS MORE AWARE OF PROBLEM

There is fortunately an increasing proportion of the profession which is alive to our problems. Complete unity is unattainable but there is a growing realization that the individual must participate in and support the organization of which he is a part.

The interpretative report of the survey was submitted to our House of Delegates and in an amateurish way we made an effort to implement it. What we did was in the right direction but could not be considered under the heading of effective therapy.

Shortly thereafter, we were confronted by the threat of Compulsory Health Insurance initiated by a governor who up to this time had given indication of a sounder attitude toward medical problems. We then sought the aid of the agency which had conducted the original survey. It was of the opinion that our situation would be better served by another type of organization and it suggested three. One was chosen, and since that time the public relations of the California Medical Association have been under professional direction.

Policy making resides in the House of Delegates and the Council of the Association. Inasmuch as the latter meets at much more frequent intervals and is more familiar with the changing picture, it usually takes the lead. The Council is advised by a committee composed of the Executive Secretary, the Legal Counsel, the Legislative Counsel and the Public Relations Counsel of the Association and the Executive Secretaries of the various County Societies having such officers. In this way, the Council is provided with the advice of a group of loyal lay employees who are experts in certain fields and most of whom have had newspaper experience. The Committee is purely advisory and has no authority to act independently. After the Council has made a decision concerning a matter which may influence public relations, the Executive Secretary of the Association acts as liaison officer to correlate the activities of those charged with carrying out the instructions of the Council. This arrangement has worked very satisfactorily.

A successful program of public relations must be based upon the worth of the group wishing to mold public opinion. Putting and keeping our house in order is the responsibility of the medical profession itself. The presentation of the viewpoint of the profession to the public is primarily the function of experts in this field, but the physicians must actively participate in this phase as well.

This was more simply stated by an acquaintance who has had considerable experience in this work, when he said, "The key to satisfactory public relations is to be 'good' or do 'good' and tell the public about it."

Our responsibility is to see that the medical profession is deserving of respect and then to see to it that the public is sufficiently informed that it will accord the profession the respect it deserves.

The basis of good public relations is primarily laid by the individual physician, whether family doctor or specialist. We all recognize that he has a dual duty to his patient. He must give to the patient the best professional care he is able, and he must treat the patient fairly in an economic sense.

There is comparatively little cause for concern on the basis of medical care. The vast majority of physicians are able and conscientious. Medical standards in this country are higher than they have been at any time and are higher than those of any other country. Medical societies, hospitals staffs and the courts provide protection for the patient in the rare instances of incompetency and neglect.

#### PHYSICIAN-PATIENT ECONOMIC RELATIONSHIPS

On the economic side, it is a rare physician who knowingly imposes an unfair financial burden upon his patient. Instances of the failure of the physician to measure up to this responsibility, however, are much more numerous than dereliction in the purely professional aspects. The economic relationship between the patient and the physician also presents an opportunity for genuine difference of opinion, and in certain instances patients are unreasonable or dishonest.

Whenever a physician treats a patient unfairly in a financial sense, he damages not only himself and the patient, but also the entire profession. It is, therefore, the concern of the profession to see that such practices are controlled.

Many county societies have established fee committees or grievance committees to which fee disputes may be referred. A better plan is to prevent disagreements from going that far.

There are two methods of approach and both should be utilized. The first is to educate the physicians concerning their responsibilities and the harm improper practices do to the entire profession. The second is the establishment of Bureaus of Medical Economics in the county societies. In California, the latter plan has been brought to greatest development in Alameda County and has been or is being instituted in all the counties about San Francisco Bay.

Briefly, the plan consists of the establishment and operation of a credit exchange and collection bureau for the members of the society. This bureau provides a variety of services to its members but the primary object is to have delinquent accounts referred to it early. The bureau then conducts an investigation of the patient and his ability to pay. It is also in a position to estimate the importance, extent and reasonable value of the services rendered. Dependent upon this investigation, it recommends what course should be followed. The ultimate decision remains in the hands of the physician concerned. He is usually agreeable to the recommendation of the bureau which makes every effort to reconcile the patient's financial status with the value of the services rendered. The patients are, likewise, pleased in most cases. The bad public relations effect of disgruntled patients loudly proclaiming that the medical profession is a group of robbers is largely obviated.

This program has reached a point in Alameda County that the county association has been able to advertise in the newspapers asking that anyone unable to obtain medical care because of inability to pay for it contact its offices. It has guaranteed to arrange for care within the ability of the individual to pay. The distinction between medical care and hospitalization has been carefully pointed out. The Bureau received three pertinent calls in response to its first campaign and none as a result of its most recent one.

Consider the public relations value of this type of advertising. It has resulted in favorable news stories and editorial comment. It has had a considerable impact upon the Legislature where a new Compulsory Health Insurance bill is pending.

#### COSTS HAVE RISEN AS CARE HAS IMPROVED

For 15 years, we have been in a period of diminishing individual responsibility and increasing governmental interest in personal welfare. While most of us are opposed to this tendency—and I heartily dislike it—we cannot afford to ignore the facts. We, as physicians, realize, probably more than any other group, the ever increasing costs of adequate medical care resulting from the continuous expansion of diagnostic and therapeutic procedures. While the major portion of the increase in cost is the result of hospital charges over which we have little or no control, it represents a part of the total bill the public is called upon to pay.

The unbudgeted expense of modern medical care constitutes the only valid argument for Compulsory Health Insurance. We know the deficiencies and consequences of socialized medicine and how bad it would be for both the patient and physician.

We also know that in the field of health insurance there is nothing government can do for the people which they cannot do for themselves, and do better and at less cost.

We may have no more moral responsibility to provide the methods of defraying the costs of medical care than have those who provide any other necessary service to the public to do the same in their own fields. Enlightened self interest, however, dictates that we do what we can to assist in the

solution of this problem. A satisfactory method must be supplied within the existing framework of private enterprise or government will step in and the result will be regimentation and bureaucratic control.

As a consequence of our public opinion survey the California Medical Association made its decision to fight socialized medicine on the basis of Voluntary versus Compulsory Health Insurance. We were successful in the 1945 Legislature but our success was based more upon future prospects than actual accomplishment. So it was necessary to implement our determination with a positive program.

The California Medical Association commenced an intensive campaign early last year to sell voluntary health insurance. This effort has been to sell not only California Physicians' Service, but also the Blue Cross plans and the policies of private carriers providing sound coverage. The California Committee for Voluntary Health Insurance was founded. Membership in this organization is restricted to non-profit plans and good insurance companies. It has conducted campaigns in 27 of our 58 counties to date.

After preliminary publicity, each campaign opens with a dinner meeting to which are invited public officials and representatives of the business, professional and employee groups. Proclamations in support of Voluntary Health Insurance are issued by the mayors of the cities in the county and endorsed by other officials, prominent citizens and groups. The objectives of the campaign are outlined and the support of the public solicited. The campaign continues for one week or longer depending upon the size of the county, and during this period extensive newspaper and radio advertising is used. The cooperation of the press has been splendid and its assistance extremely valuable. In this way, the doors are opened for the salesmen to enroll the people in voluntary programs.

The results of the first year's efforts have been amazing. California Physicians' Service membership has grown from 176,000 to 419,000. Membership in Blue Cross, with some of its containing indemnification for medical care, has increased from 350,000 to 610,000 in California. It is reliably estimated that the private insurance companies have sold between three and four policies for each subscription to California Physicians' Service. This means that the holders of sound prepayment coverage have increased more than one million and probably more nearly a million and a half in the past year.

This increase in enrollment is even more striking when it is realized that these figures were compiled before any of the more populous counties had been reached. The campaigns were begun in the smaller counties to gain experience in their conduct before they were launched in the more important areas.

#### COLLATERAL BENEFITS

In addition to the growth of the voluntary insurance program, these campaigns have built goodwill for the California Medical Association and the profession. There has been outspoken commendation of the medical profession from many sources. The campaigns have destroyed the fiction that the physicians are in opposition to progress and wish to retain a preferred position to the detriment of

In addition, the California Medical Association has maintained a weekly broadcast over a state-wide network. The subject matter of these broadcasts consists of historical anecdotes of California. The commercials announce the sponsors to be "The California Medical Association and your Family Doctor" and briefly point out the values of voluntary health insurance and California Physicians' Service.

The salesmen for California Physicians' Service state that prior to the campaigns just outlined, they spent most of their time explaining to prospects what California Physicians' Service was, but now the majority of the people to whom they talk already have some familiarity with it.

There is a close relationship between public relations and politics but the fields are not coextensive. The California Medical Association has been alert in a political sense for a considerably longer time than in a public relations sense. Medicine is definitely in politics throughout the country. Physicians naturally prefer to abstain from this field but they must come to the realization that if medicine is to remain free, they must meet their enemies in the sphere of practical politics. Few people appreciate the political force of an aroused and united medical profession. No longer can our organizations confine themselves to purely scientific matters. Our county and state societies and the American Medical Association must necessarily make their influence felt in matters which concern public health and welfare and the practice of medicine.

Projects such as those outlined are necessarily expensive. During the past year, the California Medical Association has expended more than two hundred thousand dollars. The expenditure for 1947, will be half again greater. To many, this will seem to be a very large outlay, but American Medicine is on the threshold of decision. The hour may be later than we think. Let it not be said that we were too niggardly to defend our freedom and the American way of life with sufficient force to prevent the advance of Socialism. If the keystone of

medicine falls the next pressure will push over the entire structure of free enterprise. We need only to look to the English experience. Compulsory Health Insurance came in 1912. Now 1947, barely a generation later, has witnessed the complete socialization of medicine, of the Bank of England, of the railroads, of the coal mines and of the land. In this country, Medicine has already come under attack. We cannot afford to ignore the historical parallel.

#### NO TIME FOR COMPLACENCE

We must be sure that the funds, which we handle in trust, are wisely expended so that the maximum effect may be obtained, but we must be certain that we do enough. It is far wiser to do more than necessary, than too little. We should look forward to greater efforts and expenditures rather than to complacence and economy.

We may be thankful that the recent change in the national political situation gives us more time to do our work effectively but we should not delude ourselves that this condition will continue indefinitely. We should use the time given to us to strengthen our position so that when the next as sult comes we will be better able to repel it. The advocates of Compulsory Health Insurance and Socialism are not idle. They are continuously at work looking to the time of greater opportunity.

These, then have been the experiences of the California Medical Association and the lessons to be derived from these experiences. It is not necessarily true that they apply with equal force throughout the country but in some measure they pertain everywhere. We have been unfortunate enough to be forced to face three distinct eras of determined efforts to socialize our profession. The recent attacks have been the most difficult to defeat. If we are successful in the present battle we shall have no fear of the immediate future. We shall then have built a Voluntary Health Insurance bastion against compulsion.

If our experiences and what we have learned from them can be of value to other states in meeting the same or similar problems, we shall be pleased to assist in any way we can.

490 Post Street. San Francisco.



## Some Clinical Aspects of Rheumatic Fever In the Adult on the Pacific Coast\*

MAURICE ELIASER, JR., M.D.,† San Francisco

RHEUMATIC fever is generally considered to be a disease that initially occurs in childhood, most frequently between the ages of five and twelve. 3, 6, 10, 17, 18 It is characterized clinically by fever, polyarthritis—usually migratory in type—and cardiac involvement which may or may not be readily detectable. Chorea is commonly included as a manifestation of the disease in children but is rarely found in the adult group. Other suggestive but not diagnostic criteria are tachycardia, epistaxis, subcutaneous nodules, erythema—usually either nodosum or marginatum—purpura, pneumonitis, and peritonitis. The former primarly constituted the standards by which the diagnosis was determined in the adult cases to be described.

It is now fairly universally agreed, etiologically speaking, that the disease represents an abnormal response-resembling anaphylaxis or hypersensitivity-of the host to the beta hemolytic streptococcus, most frequently group A, or its product. It implies the occurrence of a streptococcal infection preceding the onset of a rheumatic attack by about two to three weeks in a susceptible individual; the susceptibility seemingly has definite hereditary aspects, especially in the juvenile group. In rheumatic fever occurring in childhood, considerable emphasis has been placed upon familial, dietary, social, and economic factors. 11,13,14 Also geographic variations have been considered important, both as to the occurrence and the severity of the disease;1,7,12,16 that the rheumatic state can also be incurred in tropical and semi-tropical regions is now clearly recognized although it is found in these areas usually in less severe and more occult forms. It is an interesting fact that the original area of residence of the patient is of far less importance than his location at the time of incurring the disease. Militarized personnel stationed on the Pacific Coast developed a type of rheumatic fever comparable to that seen among the civilian population in the area regardless of their place of origin.

The cases to be discussed are instances of rheumatic fever as it occurs in older age groups; i.e., soldiers with an age range of 18 to 37 years, averaging 26 years. They were individuals whose period of military service varied between several weeks and three and a quarter years, averaging seven and a half months between induction and the onset of the disease. They were all sporadic cases, lacking the epidemic characteristics noted in large naval training centers as described by Jones<sup>8</sup> and others.

Because of the uniformity of living conditions among members of the Army stationed at the same post and undergoing the same training, as these were, it is obvious that many of the variables encountered in surveying rheumatic fever among civilians are eliminated, namely, the dietary, familial, environmental, social and economic factors.

The group studied consisted of 33 patients who were personally seen at an Engineer Replacement Training Center in Oregon, near Bend, at the inception of their disease in the spring of 1944 and subsequently transferred from the Station Hospital to a General Hospital in Walla Walla, Washington. They were under continuous personal observation throughout the entire course of the illness until they were either returned to duty or separated from the service—this represented six months for each patient. This group comprised 39 per cent of the total number of 85 cases followed, the second group being those with recurrent attacks of rheumatic fever. Because the problem of the recurrent case is associated with complicating factors as to etiology, clinical course, etc., it is not being discussed here in detail.

We were aware of the difficulty involved in deciding which is the *initial* attack of rheumatic fever, especially on the Pacific Coast where the joint manifestations are so often mild; and also that about 30 per cent of all persons suffering from rheumatic heart lesions are not aware of their ever having had the acute disease.<sup>17</sup> It is believed, however, that the present group primarily represents initial attacks. This will be fairly well shown when we review the prodromal disease leading up to the onset of rheumatic fever.

The majority of the new cases were of the monocyclic type which is consistent with the findings of Griffith<sup>5</sup> and others, who observed the disease among naval personnel in California.

#### GEOGRAPHIC ASPECTS

Regarding the geographic aspects of the disease on the Pacific Coast, it was found that its characteristics were practically identical in Oregon and California where we observed another series of rheumatic patients who were hospitalized at Santa Barbara. Furthermore, these two groups were strikingly comparable to a series of 20 adult civilian shipyard workers who developed rheumatic fever in the San Francisco Bay area. 15

The histories of the patients in the Oregon group did not reveal any consistent family history of rheumatic fever. The patients were not found to represent an underprivileged group either socially or economically, and questioning as to previous civilian occupation revealed nothing of significance.

Of the 33 patients, only three had scarlet fever

<sup>\*</sup> Read before a Joint Meeting of the California Medical Association and the California Heart Association, Los Angeles, May 10, 1946.

From the Division of Medicine, University of California Medical School, San Francisco, California.

<sup>†</sup> Formerly Lt. Col., MC, AUS.

during childhood or adolescence, which was significantly lower than a control group of 100 non-rheumatic patients of the same age range. The incidence of recurrent spontaneous epistaxis was 30 per cent compared with 11 per cent in the controls. This variation is of some interest because of the recent tendency to discount the significance of nose bleeding among juvenile rheumatic fever patients.

Only two patients presented histories of previous asthma; the remainder failed to describe any symptoms that could have been considered to be of an allergic type. This may indicate that the hypersensitivity of streptococcal origin differs from clinical allergy as we now recognize it.<sup>9a</sup>

Twenty-seven per cent of the patients had had their tonsils removed, compared to 33 per cent of the control group. This suggests the questionable value of the procedure prophylactically, as has been repeatedly shown in large series of juvenile cases in New England and elsewhere.

The type of disease that was assumed to be causally related to the onset of rheumatic fever is shown in Table 1. The examples of pneumonitis

Table 1.—Type of Premonitory Disease and Time Interval Preceding Onset of Clinical Manifestations of Acute Rheumatic Fever

Premonitory Disease			ber of	Average Days Between Premonitory Disease and Rheumatic Fever
Tonsillitis Pharyngitis	.18	(	55%)	13.4
Scarlet Fever	. 6	(	18%)	19.0
Arthralgia	. 5	(	15%)	
Acute Upper Respirator Infection	y . 2	(	6%)	21.0
Preumonitis	. 2	(	6%)	17.5

Total: 33 Average: 17.7

probably did not represent intrinsic pulmonary rheumatic involvement because of the interval elapsing between the two diseases.

Incidentally none of these patients attributed the onset of rheumatic fever either to exposure, dampness, or to unusual fatigue. However, among the 55 patients who developed recurrent attacks, 47 per cent related their attacks to one or the other or all of these. Likewise the premonitory conditions which preceded the onset of acute and recurrent rheumatic fever differed, as shown in Table 2.

Physical examination did not reveal any evidence that there was a disproportionate number of patients with blond or red hair or blue eyes as has been suggested among juvenile rheumatic individuals, and no consistent body conformation was noted among the affected adults.

Generalized lymphadenopathy was detected in 88 per cent of the patients at the height of the dis-

ease. It has been previously reported that lymphadenitis is even more common among the juvenile than the adult individuals.9b

No instance of erythema nodosum or marginatum was found. This is consistent with the concept that the skin is an important shock organ among children suffering from any disease associated with abnormal sensitization. Also erythema nodosum is known to occur ten times more frequently among women than men so and the present series represents only the adult male.

The joints involved were primarily the major ones, the ankles, knees, shoulders and elbows being most commonly affected, in that order. The belief that extensive articular involvement precludes cardiac disease was not substantiated. Although in some instances the joint manifestations were prominent features at the onset, very rarely did they attain the degree of swelling, redness, and immobility so commonly seen among children, especially in such highly endemic areas as New England and the Rocky Mountain States. Actually, relatively mild articular disease has been characteristic on the Pacific Coast among all age groups, which may well account for the apparent frequency of missed acute cases. The occasional occurrence of symmetric fusiform swelling of the proximal interphalangeal ioints associated with extensive carditis substantiated the clinical belief that involvement of the small joints is of serious import in the adult as well as in the child.

#### PRESENCE OF SIGNIFICANT CARDIAC MURMURS

Significant cardiac murmurs were detected in 15, or 45 per cent, of the patients at the onset of the arthritic phase of the disease. In five of these patients the murmurs had receded by the time of clinical quiescence. Of the 18 without valvulitis, only one patient developed a significant cardiac murmur during the acute phase of the disease.

Five examples of murmurs originally of important intensity that disappeared during convalescence were encountered. This raised the usual question of the difficulty in evaluating any cardiac murmur during the acute rhase of the disease. However, in the adult, among whom the condition occurred with relatively low fever, mild tachycardia, and less pronounced systemic manifestations, the finding of any cardiac murmur cannot be so lightly considered as those in the acutely ill, markedly febrile child (Tables 3 and 4).

Regarding laboratory data, procedures were carried out in an attempt to establish the specific group and type of streptococcus involved in causing the acute as well as the recurrent episodes. Likewise antistreptolysin titer determinations were

Table 2.—Comparison of Premonitory Disease Preceding Clinical Manifestations of Acute and Recurrent Rheumatic Fever

Scarlet Fever	Tonsillitis Pharyngitis	Arthralgia	Acute Upper Respiratory Infection	Appendicitis
Acute18.0%	54.0%	15.0%	12.0%	
Recurrent 3.3%	16.7%	63.6%	10.0%	7.7%

obtained in many instances. For practical purposes the erythrocytic sedimentation rates proved to be of greatest clinical value. The range in the acute cases was between 27 and 60 mm. per hour by the Wintrobe method, in which method 0-9mm. is considered normal. The average rate at the time of admission to the hospital was 47 mm. per hour.

TABLE 3 .- Cardiac Involvement at Onset of Disease

No demonstrable	valvulitis	(EA ERL)
No demonstrable	varvuntis	(04.0%)
Mitral valvulitis		(27.2%)
Mitral and aortic	valvulitis 4	(12.1%)
Aortic valvulitis		( 3.1%)
Pancarditis		(3.1%)

Table 4.—Incidence of Lesions Among 15 Patients with Clinically Demonstrable Heart Disease

					-							
Mitral	involvement	alone									 	60.0%
Aortic	involvement	alone									 	 6.7%
Mitral	and aortic	involve	men	t							 	 26.6%
Perica	rditis					 	 				 . ,	 6.7%

It was arbitrarily assumed that the acute phase had been terminated when the sedimentation rate reached 10 mm., if not associated with subjective or other objective evidence of activity. By these standards the average duration of the disease was 63 days, compared with the average of six months usually reported among invenile patients. An incidental observation was that those patients whose sedimentation rates were more rapid at the onset frequently had a shorter course than the low-grade subclinical group who often had lower initial rates and more prolonged periods of activity.

#### RARE EVIDENCE OF PSYCHONEUROSIS

An interesting observation among the acute rheumatic adults was that they exhibited evidence of psychoneurosis very rarely. This was quite striking when these patients were compared with soldiers complaining of joint pain due to other causes. As a preliminary differential point in ruling out so-called psychogenic rheumatism, it was of almost diagnostic significance. Likewise it emphasized the importance of carefully evaluating the persistent arthralgia which occasionally follows the subsidence of the acute phase of rheumatic fever, in the absence of radiographic or other objective signs.

During the period of initial observation of patients with rheumatic fever it was repeatedly found that soldiers complained of mild joint pains without demonstrable articular involvement. These could easily have been erroneously considered to have been without organic basis if further investigation had been omitted. Careful questioning, cardiac examination, determination of the sedimentation rate and electrocardiography were necessary to evaluate properly the condition.

The electrocardiograms were of considerable interest in this series of cases. They revealed the alterations of intra-auricular and auriculo-ventricular conduction which are well known. In addition, a large number of abnormalities of the ST-segment

were noted which were considered to be of possible diagnostic significance.

As for prognosis, of the military groups studied in the Pacific Northwest and Southern California, approximately 35 per cent were returned to duty in accordance with the then established army criteria for apparent quiescence. The various reconditioning programs were of definite value in completing convalescence. Actually there is reason to believe that no one should continue to remain in military service after he has proved to be a sensitized individual, regardless of the presence or absence of demonstrable cardiac complications.

Therapeutically, sodium salicylate was generally employed in daily doses of 10 to 12 gm., with the usual prompt response noted in children. The question of concomitant administration of sodium bicarbonate is still debatable but there is good reason to believe that it lowers the desired blood levels of saliculate by reducing absorption and increasing renal excretion of the drug and that, contrariwise. acidic urine reduces renal excretion and thereby raises the blood levels.2 In those persons who were unable to tolerate the drug by mouth, the administration of an 1 per cent aqueous solution of sodium salicylate intravenously for the first day or two was found to be quite safe when given slowly. We did not believe that we had observed our patients sufficiently long to ascertain whether prolonged high salicylate blood levels actually reduced the incidence of late cardiac complications as has been suggested.4 Penicillin did not alter the course of the disease.

We encountered several examples of the well-known deleterious effect that the sulfonamides have upon an attack of rheumatic fever. Not only do they lack any beneficial therapeutic effect but seemingly they aggravate the condition. There is currently considerable discussion as to the mechanism involved, but, regardless, it is safe to say that the use of this group of drugs is clearly contraindicated during the active phase of the disease.

Prophylactically it has been well established that small doses of sulfadiazine given over prolonged periods of time will reduce the incidence of recurrent attacks of rheumatic fever in adults and children. In adults 1.0 gm, is an adequate daily dose.

In summary it can be said that rheumatic fever, as it occurs in adults on the Pacific Coast, presents a diagnostic challenge. The relatively mild nature of the acute arthritic phase of the disease coupled with the significantly high incidence of cardiac disease warrants serious consideration.

It is appreciated that during and following streptococcal infections, especially those of group A, some persons will develop carditis without arthritis. Nevertheless, critical evaluation by physical, diagnostic, laboratory, and electrocardiographic methods is essential if one were to explain the paradox on the Pacific Coast that rheumatic fever is rather rare, but rheumatic heart disease is fairly common.

#### SUMMARY

1. The study of acute rheumatic fever among adults who were members of the armed forces re-

vealed that there were several differences that distinguished it from the juvenile form.

- 2. Military life is such that dietary, familial, social and economic conditions are fairly constantly eliminated as influencing factors in the initial attack of the disease. This is especially true in a group of soldiers undergoing identical training at the same camp.
- 3. Hemolytic streptococcal infections, including scarlet fever, are common precursors of the acute disease in the adult and are followed by a two- to three-week period during which extremely strenuous physical activities do not produce symptoms.
- 4. Clinically significant cardiac murmurs were audible in 45 per cent of the patients at the onset of the disease. Probable valvulitis was revealed in 15 per cent at the onset but was not detectable following convalescence.
- 5. The involvement of joints among adult patients developing their initial attack in the Pacific Coast area is relatively mild compared to that described in children in several other parts of the United States.
- 6. The duration of the active phase of the disease averaged 63 days, using all the accepted clinical and laboratory methods to determine activity.
- 7. There is absence of psychoneurosis among patients with acute rheumatic fever. This fact is striking when compared with cases of arthralgias of other types in military personnel.

#### REFERENCES

- 1. Bilderback, J. B. and Overstreet, R. M.: Incidence of Rheumatic Infections in Children of Oregon, Northwest Med., 37:390-393 (Dec.), 1938.
- 2. Caravati, C. M. and Cosgrave, E. F.: Salicylate Toxicity: Probable Mechanism of Its Action, Ann. Int. Med., 24:683-643 (April), 1946.

- 3. Cheadle, W. B.: Lectures on the Practice of Medicine, London, Smith, Elder & Co., 1900, p. 227.

  4. Coburn, A. F.: Salicylate Therapy in Rheumatic Fever; Rational Technique, Bull. Johns Hopkins Hosp., 73:435-464 (Oct.), 1943.
- 5. Griffith, G. C.: Rheumatic Fever: Its Recognition, Calif. & West. Med., 63:119-123 (Sept.), 1945.
- 6. Hedley, O. F.: Rheumatic Heart Disease in Philadelphia Hospitals. II—Age, Race and Sex Distribution and Interrelation of Rheumatic Fever, Sydenham's Chorea, Rheumatic Heart Disease, and Subacute Bacterial Endocarditis, Pub. Health Rep., 55:1647-1691 (Sept. 13), 1040.
- 7. Jones, T. D.: Heart Disease in Childhood, Am. J. Pub. Health, 28:637-643 (May), 1938.
- 8. Jones, T. D., cited by Paul, J. R.: Epidemiology of Rheumatic Fever, sec. ed., New York, Metropolitan Life Insurance Co., 1943, p. 38.
- 9. Lichtwitz, L.: Pathology and Therapy of Rheumatic Fever, New York, Grune & Stratton, 1944. (a) p. 25; (b) p. 148; (c) p. 112.

  10. Mackie, T. T.: Rheumatic Fever; Analytical Study of 393 Cases of Rheumatic Fever and 89 Cases of Chorea, Am. J. M. Sc., 172:199-221 (Aug.), 1926.
- 11. Miller, R.: Report on Environmental and Other Predisposing Causes of Rheumatic Infections, Brit. M. J. (supp.), 2:5-10 (July 3), 1926.
- 12. Mills, C. A.: Medical Climatology, Springfield, Ill., Charles C. Thomas, 1939, p. 213.
- 13. Paul, J. R.: Environmental Factors in Rheumatic Fever, Tr. Am. Physicians, 55:290-293, 1940.
- 14. Rinehart, J. F.: Studies Relating Vitamin C Deficiency to Rheumatic Fever and Rheumatoid Arthritis; Experimental, Clinical and General Considerations; Rheumatic Fever, Ann. Int. Med., 9:586-599 (Nov.), 1935.
- 15. Sellers, A. L. and Levine, E. B.: Acute Rheumatic Fever in Adults, Permanente Found. M. Bull., 3:81-86 (April), 1945.
- 16. Shapiro, M. J.: Natural History of Childhood Rheumatism in Minnesota, J. Lab. & Clin. Med., 21:564-573 (March), 1936.
- 17. White, Paul D.: Heart Disease, sec. ed., New York, MacMillan Co., 1942, p. 233.
- 18. Wilson, M. G., Lingg, C., and Croxford, G.: Statistical Studies Bearing on Problems in Classification of Heart Disease; Heart Disease in Children, Am. Heart J., 4:164-196 (Dec.), 1928.



## The Electrocardiogram in the Diagnosis And Management of Rheumatic Fever\*†

MAURICE SOKOLOW, M.D., San Francisco

THE diagnosis of rheumatic fever in adults has at times been difficult because of atypical clinical features. Jones has indicated the following list of criteria for diagnosis, of which carditis is the major manifestation:

#### 1. Major manifestations:

Carditis, arthralgia, chorea, nodules, and verified history of previous rheumatic fever.

#### 2. Minor manifestations:

Fever, abdominal or precordial pain, ervthema marginatum, epistaxis, pulmonary changes, and laboratory abnormalities.

In adults, chorea and nodules are rare, and a verified history of rheumatic fever is difficult to obtain. Of the major manifestations, therefore, one is dependent on arthralgia and carditis. Arthralgia is often absent, or may be minimal, subjective or monarticular. Its interpretation is at times difficult, but when associated with carditis, its significance becomes clear.

Carditis, then, is the outstanding major manifestation to be searched for in rheumatic fever in adults. It may be recognized by cardiac enlargement, cardiac failure, acute pericarditis, significant murmurs or significant electrocardiographic abnormalities. Of these evidences of carditis, only murmurs and electrocardiographic abnormalities are common in rheumatic fever in the adult; of the murmurs, diastolic murmurs are unequivocal but uncommon; and systolic murmurs are difficult to evaluate and are often heard in febrile diseases without carditis. Therefore one must depend largely on electrocardiographic abnormalities as the most common evidence of carditis.

Minor changes in the electrocardiogram must be evaluated carefully, and the widening range of normal variants considered before interpreting such changes as indicative of carditis. The following table shows (a) the frequency with which various abnormalities in the electrocardiogram were observed among 700 cases studied at the U.S. Naval Hospital, Oakland, California, and (b) the duration of the A-V block in 76 cases:

Total cases of rheumatic fever...... 700 Total cases of abnormalities in the electrocardioa. Of the 147 cases: 1. Conduction defect ..... 88 A-V block ..... 86 I-V block ..... 2 2. Significant T wave changes...... 52 3. Miscellaneous (including abnormal b. Duration of A-V block in 76 cases: 9-14 days ..... 39

Some of the changes noted such as nodal rhythm, axis changes, P wave changes, etc., might be controversial, but definite partial A-V block and diphasic or inverted T waves are considered significant. The high incidence of significant T wave changes in the absence of clinical signs of acute pericarditis is noteworthy.

15—28 days ..... 20

Over 3 months .....

A-V conduction defects, the most common abnormality found (60 per cent), have been frequently discussed. Such a conduction defect may manifest itself as delayed A-V conduction, complete A-V dissociation, partial A-V block with dropped beats, or partial progressive A-V block with Wenckebach phenomenon. To be of diagnostic value, a delayed A-V conduction should have a PR interval of at least 0.20 sec., with due consideration of the cardiac rate. On the other hand, some cases will be missed with this criterion in mind, because it has been observed that a PR of 0.18 or 0.19 sec., seen at the onset of the disease, may shorten to 0.12 or 0.13 sec. as the patient improves. The former figure, while in the normal range, thus, in retrospect, may prove to be abnormal for the particular patient. Unless unequivocal evidence of rheumatic fever was present, no diagnosis of carditis was made in our series of cases, unless a decrease of at least 0.04 sec. occurred in the PR interval with clinical improvement.

The changes in the PR interval may be surprisingly transient and intermittent, and the frequency of abnormal tracings depends on the frequency with which electrocardiograms are taken.

#### CASE REPORT

The following case report illustrates the point in question.

Case I. W.C.J., Y 3/c, age 19, was admitted to the U.S. Naval Hospital, Oakland, on March 22, 1945. He had had

<sup>\*</sup> Read before a Joint Meeting of the California Medical Association and the California Heart Association, Los Angeles, May 10, 1946.

From the Division of Medicine, University of California Medical School, San Francisco, California.

† This article has been released for publication by the Division of Publications of the Bureau of Medicine and Surgery of the U. S. Navy. The opinions and views set forth in this article are those of the writer and are not to be construed as reflecting the policies of the Navy Department.

<sup>‡</sup> Formerly Lt. Comdr. (MC) U.S.N.R.

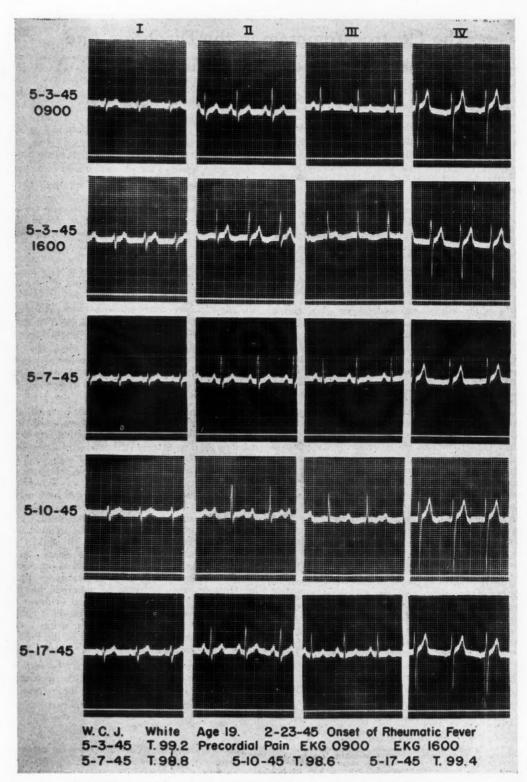


Figure 1.—Transient conduction defects in rheumatic fever.

an attack of rheumatic fever with polyarthritis 18 months before, which lasted two weeks. He developed arthritis of the ankles on February 23, 1945, while aboard ship in the South Pacific, without previous upper respiratory infection. At that time an elevated blood sedimentation rate (B.S.R.) of 26 mm. per hour\* was found, but examination of the heart, and an electrocardiogram were normal. He was placed on salicylates and transferred via several naval activities to the United States. During the transfer, this medication was stopped and he developed arthritis of the right knee.

On examination on March 22, 1945, he had a temperature of 101.2°F. and polyarthritis of the ankles and of the right knee. Examination of the heart was negative. The B.S.R. was 29 mm. per hour. Three electrocardiograms taken at intervals were normal with a PR of 0.16 sec. until April 9, when a partial A-V block with a PR of 0.40 sec. was found. Four days later the PR was again 0.16 sec. On May 3, he complained of precordial pain and aching of the right knee, but an electrocardiogram taken at 9:00 in the morning was normal with a PR of 0.16 sec. At 4:30 in the afternoon of the same day the PR was 0.36 sec. This partial A-V block persisted for four days until May 7, when it was again 0.16 sec. Three days later the PR was 0.36 sec., and a week later the electrocardiogram was normal (Figure 1). During the period in which the vari-

able transient partial A-V block was observed, the patient had frequent bouts of lowgrade fever to 100.4°F. (Figure 2) despite full doses of salicylates. The B.S.R. remained elevated between 19 and 30 mm. per hour, until August 19, five months later, when it fell to 6 mm. per hour. The electrocardiogram remained normal between May 7 and June 7, but on the latter date the PR was noted to be 0.44 sec. A week later it was again 0.16 sec. and remained at that figure until August 16, when it was 0.14 sec. On September 20, he was transferred to a convalescent hospital.

Comment. This interesting case illustrates the chronic active form of rheumatic fever resembling that so often seen in children. The repeated episodes of transient partial A-V block, at times lasting only a few days, is noteworthy. The changes from a normal electrocardiogram to a PR of 0.40 sec. within a period of  $7\frac{1}{2}$  hours as seen on May 3, emphasizes how a partial block may be missed unless frequent tracings are made.

#### T WAVE CHANGES

T wave changes have been mentioned in the literature but have not been given the close attention that the frequency of their occurrence merits. Most writers have commented solely on the change in the T waves in association with acute pericarditis.

<sup>\*</sup> Westergren method used throughout.



Figure 2.—Course of chronic active rheumatic fever with subclinical polycyclic episodes.

Lowering of the T waves, unassociated with tachycardia, is difficult to evaluate and while suggestive, has not been termed a significant electrocardiographic abnormality. The T wave changes are not so likely to be intermittent as the PR changes, but may be surprisingly transient. When serial records are taken, progressive changes toward normal occur through the diphasic, flat, and low T wave stages. Leads I, II and IV are usually all involved, as shown by early records; however, depending on the stage of recovery, abnormalities may be seen in single leads only, especially in lead IV. Due care for the position of the apical electrode with multiple precordial leads must be taken to evaluate changes in lead IV alone.

In addition to being helpful in the initial diagnosis of rheumatic fever, the electrocardiogram aids in following the course of the disease and in influencing its management. Polycyclic rheumatic fever has a more serious prognosis in terms of residual cardiac effects. Many polycyclic phases are subclinical, the patient being unaware of the renewed activity, even in the presence of fever. Ab-normalities in the electrocardiogram may reappear, making the recrudescence of carditis objective. After the disease is considered to be quiescent and the patient is allowed up he should still remain under close observation, and frequent electrocardiographic studies made and the blood sedimentation rates observed. We have seen recrudescences, first discovered by the appearance of electrocardiographic changes, even before the patient was aware of symptoms and at times before a higher B.S.R. and other signs of activity reappeared.

#### CASE REPORT

A case report illustrating the foregoing observa-

Case 2. J.W.B., S 1/c, age 18, was admitted to the Naval Hospital, Oakland, on January 26, 1945. Four days prior to entry he had noted pain in the arches of both feet which increased in severity and was associated with stiffness; on the day before entry he also noted slight swelling of the ankles. He had been very active prior to the onset and had had no constitutional symptoms except for moderate anorexia for the previous two days. There was no history of any previous attacks of rheumatic fever and no upper respiratory infection.

On arrival he complained of pain in his feet and right knee. The temperature was 102°F., pulse 112, respiration 18. The pertinent findings were confined to the joints and there was redness, tenderness and slight swelling of both ankles and of the toes. The right knee was stiff but not swollen. The heart was negative, as were the urine and blood Kahn.

The patient was put to bed but no salicylates were given. Three days after entry he developed pain in the right knee and in the shoulders and a rash diagnosed as erythema marginatum appeared over the thorax. The temperature was  $100.6^{\circ}$ F. The heart was slightly enlarged to the left, the heart sounds were muffled and distant and there now was a grade 2 blowing apical systolic murmur. No rub was heard and the patient had no precordial pain. The B.S.R. was 25 mm. per hour and the electrocardiogram revealed a flat  $T_2$  and inverted  $T_1$  and  $T_4$  (Figure 3). He was given 10 grams of salicylates and observed.

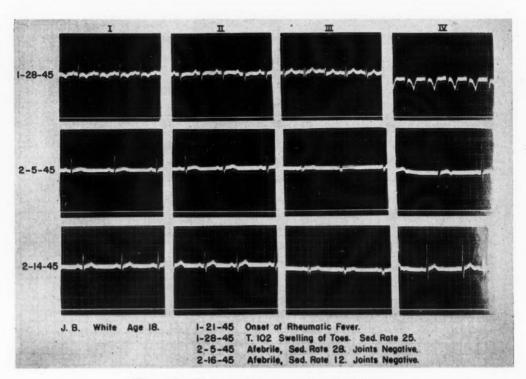


Figure 3.—T wave changes in rheumatic fever.

His temperature and pulse became normal within four days (Figure 4). His joint pains subsided more gradually but two weeks after entry he was entirely asymptomatic and the rash had disappeared. The heart sounds were fair, but more distinct. The apical systolic murmur was faint. The B.S.R. fell slowly, reaching 6 mm. per hour on March 8, 41 days after entry. The electrocardiogram became progressively normal. The total duration of the abnormal T waves was 19 days.

Comment. This case illustrates the typical usual sequence of T wave abnormalities in rheumatic fever, and the fact that they occur independently of A-V conduction abnormalities. The changes in the T waves are indistinguishable from those seen in pericarditis and it is believed that they are probably due to pericarditis which is not detectable clinically. The frequency with which pericarditis is noted pathologically is much greater than its clinical diagnosis because of the absence of diagnostic signs differentiating pericarditis from myocarditis in rheumatic fever. Myocarditis, without pericarditis, could cause the T changes and probably is in part responsible, but the serial changes strongly suggest a pericardial origin.

Residual activity. A real problem presenting itself occasionally is that in which residual electrocardiographic changes persist after all other signs of activity have subsided. The problem arises as to whether to allow the patient up in the presence solely of residual electrocardiographic abnormalities. Although some have questioned it, the most accepted procedure is to keep the patient in bed until all signs of activity have disappeared. Our policy has been to allow such a patient up, but keeping careful electrocardiographic control. In those patients in whom the residual electrocardiographic abnormalities indicated continued rheumatic activity, the tracing became more abnormal and other signs of activity such as an elevated sedimentation rate reappeared. If no recrudescence occurred with activity of the patient, he was allowed progressively to assume full activity. With this procedure, approximately 4 per cent of those patients with electrocardiographic abnormalities, or less than 1 per cent of the total rheumatic group, had fixed residual electrocardiographic changes, months after the disease became quiescent.

#### CASE REPORT

A case report illustrating such residual signs follows.

Case 3. J.R.J., S 2/c, age 18, was admitted to the Naval Hospital, Oakland, on March 6, 1945. His records showed

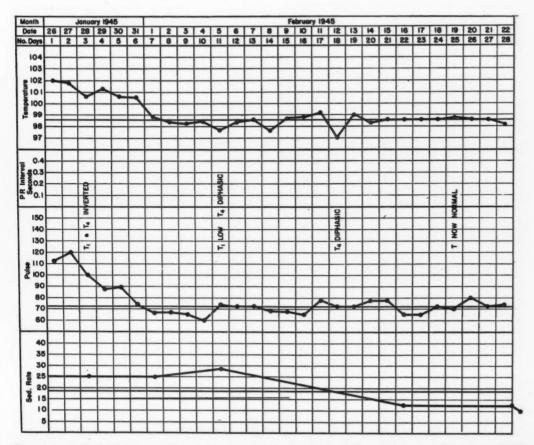


Figure 4.—Clinical course of monocyclic rheumatic fever with only T wave changes in ECG.

that he had had a febrile sore throat and tonsillitis on January 6, 1945, and he was hospitalized for a week. On January 18, he reported again to his sick bay because of the sudden onset of swelling and pain in his left knee. At that time he had a temperature of 101.2°F., the B.S.R. was 27 mm. in 30 min., but the heart was negative. He was treated with sulfadiazine and penicillin, but his fever and joint pain persisted and on January 23 he was placed on salicylates. Four days later he was afebrile and the knee was much improved. No electrocardiographic tracings were made. He was allowed up and his medication was stopped. By February 9, two weeks later, his B.S.R. had increased to 24 mm. per hour and an electrocardiogram revealed a partial A-V block with a PR of 0.28 sec. He was given 4 gm. of salicylates daily and put to bed. His B.S.R. was 21 mm. per hour on February 15, and 13 mm. on February 27. On March 1, his PR was normal and he was again allowed up and was transferred to the Naval Hospital, Oakland, on March 6, 1945.

On arrival he had no complaints, was afebrile, had a cardiac rate, in bed, of 63, there was no cardiac enlargement and no murmurs were heard. The joints were negative, both subjectively and objectively. The tonsils were enlarged as were the cervical lymph nodes which were also slightly tender. The laboratory data revealed a normal urine and negative blood Kahn. The hemoglobin was 78 per cent, the white blood cell count 13,200, with 62 per cent polymorphonuclear cells. The B.S.R. was 19 mm. per hour. The electrocardiogram revealed a partial progressive A-V black with Wenckebach phenomenon. The PR was 0.30 sec.

The patient was kept in bed and given 10 gm. of salicylates daily. He remained asymptomatic and afebrile and there were no abnormal findings in the skin, heart or joints. The B.S.R. fell to 8 mm. per hour in four days and throughout March and April his B.S.R. varied from 3 to 8 mm. per hour. Electrocardiograms taken twice a week revealed partial A-V block in all, the PR varying from 0.22 to 0.36 sec. Dropped beats and Wenckebach phenomenon were occasionally noted. Salicylates were finally stopped on April 23, 1945, after seven weeks of observation. His pulse varied from 60 to 80 and on May 20 he was allowed up because the only sign of activity was the partial A-V block and this had been present as the only objective sign for over two months. Further, no symptoms had appeared for a month after the omission of salicylates. Within a week, on May 28, his cardiac rate in bed had increased from 60 to 96, his temperature was 99.2°F., the B.S.R. had increased to 15 mm. per hour, and the PR from 0.22 to 0.28 sec. It was felt that these changes indicated continued rheumatic activity and he was returned to bed and transferred to a convalescent hospital.

Comment. This most interesting case illustrates: monarticular arthritis in rheumatic fever; subsidence of the B.S.R. in six weeks despite continued partial A-V block; recrudescence upon physical activity after the B.S.R. had been normal for two months, salicylates omitted for one month, and all signs of activity absent except for a PR of 0.22 to 0.24 sec. In this case, the slightly prolonged PR interval must be interpreted as indicating residual rheumatic activity. Unfortunately, final observation was not possible.

#### SUMMARY

The electrocardiogram is of major value in the diagnosis of rheumatic fever, in determining the presence of a polycyclic course, and in detecting subclinical recrudescences when the patient is allowed up. The electrocardiographic abnormalities represent the most common manifestation of carditis in adult rheumatic fever and enable one to identify obscure arthralgia or other poststreptococcic illness as rheumatic fever. These manifestations, in 95 per cent of the cases, are partial heart block and significant T wave changes. The recent work of Rantz and his associates,2,3 and of Watson and his associates4 has shown that following hemolytic streptococcic respiratory infections, some patients have the classic type of rheumatic fever. Others, however, have minimal or atypical manifestations of illness which were shown to be associated with electrocardiographic abnormalities indistinguishable from rheumatic fever. In clinical practice one sees such atypical cases, and frequent electrocardiograms are of inestimable value in determining the true significance of the clinical manifestations.

#### REFERENCES

- 1. Jones, T. D.: The Diagnosis of Rheumatic Fever, J.A.M.A., 126:481-484 (Oct. 21), 1944.
- 3. Rantz, L. A., Boisvert, P. J., and Spink, W. W.: Etiology and Pathogenesis of Rheumatic Fever, Arch. Int. Med., 76:131 (Sept.), 1945.
- 3. Rantz, L. A., Spink, W. W., and Boisvert, P. J.: Abnormalities in the ECG Following Hemolytic Streptococcus Sore Throat, Arch. Int. Med., 77:66 (Jan.), 1946.
- 4. Watson, R. F., Rothbard, S., and Swift, H. F.: The Relationship of Postscarlatinal Arthritis and Carditis to Rheumatic Fever, J.A.M.A., 128:1145-1152 (Aug. 18), 1945.



## The Differential Diagnosis of Adult Rheumatic Fever and Rheumatoid Arthritis\*

EPHRAIM P. ENGLEMAN, M.D., San Francisco

THE differential diagnosis of rheumatic fever and rheumatoid arthritis is said to be easy. But this refers to textbook cases which do not always occur in practice. As a matter of fact, experience during the last war has stressed the difficulties encountered in the differentiation between these two diseases. The importance of carditis in the diagnosis of rheumatic fever<sup>11</sup> cannot be over-emphasized. However, it has been long recognized that in adult rheumatic fever signs of carditis may be entirely absent or of such a fleeting nature that they are overlooked. For example, of a series of 415 cases of adult rheumatic fever, definite carditis could not be demonstrated in 40 per cent, despite frequent electrocardiographic and other studies.6 Failure to demonstrate carditis, then, may be one reason for diagnostic difficulties.

Rheumatoid arthritis with its prodromal constitutional symptoms, followed by an insidious onset and slow progression of joint manifestations is an easily recognized entity. But the type of rheumatoid arthritis causing the greatest diagnostic confusion does not fulfill the classic description. As many as 10 per cent of the patients admitted into army centers for rheumatic fever were later found to have chronic joint disease clinically similar to rheumatoid arthritis.

It is currently believed by most American workers1,3,9 that these cases are examples of the acute, "atypical" form of rheumatoid arthritis. With its sudden onset this type of rheumatoid arthritis may be of varying severity and it may or may not be followed by a symptomatic remission. If observed long enough, these patients will usually show frequent recurrences or exacerbations and sooner or later will merge into the more characteristic clinical picture of rheumatoid arthritis. The development of chronic arthritis following an initial illness which simulates rheumatic fever is one reason for the opinion 4,7,8 that rheumatoid arthritis may be a residue of and secondary to rheumatic fever. However, the common pathogenesis of these two diseases has never been established. Nor is it likely that such a controversial concept can be definitely accepted or rejected until the etiology of both diseases is known. In the meantime we may regard these as separate entities and every effort should be made clinically to differentiate between them. The prognostic and therapeutic implications of early, accurate diagnosis are all too clear.

It would appear, then, that the problem at hand resolves itself into how one may distinguish be-

tween adult rheumatic fever without carditis and acute, atypical rheumatoid arthritis. It is this question that the following study has attempted to answer. A clinical comparison has been made of patients who, admitted into Army Service Forces rheumatic fever centers, were later discharged with a diagnosis of either rheumatic fever or rheumatoid arthritis. For this purpose the selected rheumatic fever patients have been limited to those with evidence of carditis, either permanent or transitory, and exclusive of the transient systolic murmur. For comparison only those cases of rheumatoid arthritis showing characteristic joint x-ray findings have been included. While these findings are not thought of as prerequisites for correct diagnosis, they are sound and objective diagnostic criteria upon which a comparative study such as this must be based. Two hundred fifty-two patients with rheumatic fever and with significant carditis, as defined above, have been compared with thirty-three soldiers, who, admitted with a diagnosis of rheumatic fever, were later considered to have atypical rheumatoid arthritis with diagnostic x-ray changes. All patients were observed for from six to fifteen months. Significant similarities and dissimilarities between these two groups are now presented.

#### AGE RANGE OF PATIENTS

The average age of the patients with rheumatoid arthritis was 28.4 years, some four years older than that of the rheumatic fever patients. However, the age range, as well as the distribution of sex and color, was the same in both groups. The youngest patient in either group was 18 years. The oldest rheumatoid was 39 years old, while the oldest individual with rheumatic fever, a dental officer in his initial attack, was 45 years of age. A history of at least one attack of previous polyarthritis was obtained in 40 per cent of the rheumatic fever pa-tients and in 57 per cent of the rheumatoids. The available data concerning their past illness were in most cases insufficient for proper diagnostic appraisal.

An incident of some significance was the antecedent sore throat or upper respiratory infection. (Table 1.) Seventy-two per cent of the rheumatic fever patients gave such a history seven to twentyeight days before the onset of joint symptoms, while only 9 per cent of the rheumatoids gave a similar

TABLE 1 .- Antecedent Upper Respiratory Infection in Adult Rheumatic Fever and "Atypical" Rheumatoid Arthritis

		RF	RA
Ifornia Heart Association at the	Antecedent URI	81%	24%
the California Medical Associa-	7-28 days before onset	72%	9%
7-10, 1946. rofessor of Medicine. University	Less than 7 days before onset	9%	15%
School; Chief, Arthritis Clinic,	No antecedent URI	19%	76%

<sup>\*</sup>Read before the California Heart 75th Annual Session of the Californ tion, Los Angeles, May 7-10, 1946. † Assistant Clinical Professor of 1 of California Medical School; Chie Mount Zion Hospital, San Francisco.

history. Fifteen per cent of the rheumatoids complained of a preceding upper respiratory infection within three days or less, while 76 per cent denied any such event. Both the antecedent respiratory infection and its time relationship with the onset of articular symptoms are worthy of attention.

Two hundred four, or 81 per cent, of the patients with rheumatic fever and all of those eventually diagnosed as atypical rheumatoid arthritis showed objective evidence of joint disease, including intraor peri-articular effusions. In both groups of cases the initial joint symptoms were most often referable to one of the weight-bearing articulations, usually the knee or ankle with subsequent symmetrical, polyarticular involvement. Contrary to what might have been expected, the polyarthritis of adult rheumatic fever was migratory in only 37 per cent of those patients on whom adequate data were available, whereas in the remaining 63 per cent the arthritis was of a progressive nature in that the symptoms and signs, in previously affected joints, persisted for the duration of the arthritis. Among the rheumatoids the arthritis was always progressive. The average duration for the development of the polyarthritis of rheumatic fever was 6.4 days, while among the rheumatoids the development was considerably slower, an average of 19.1 days. At the climax of the polyarthritis the distribution of joint affection was the same in both groups, with small joint involvement of the fingers and toes in approximately one-half of the patients.

The remarkable effect of salicylates in rheumatic fever has been long recognized.12 In adult rheumatic fever, however, one must distinguish between the subjective joint response to salicylates and the objective response, specifically the rate at which joint swelling disappears. It was not unusual for rheumatic fever patients to continue to experience joint pains for several months despite adequate salicylates. But joint effusions usually disappeared in a few days, and never more than 18 days, provided the patient was properly treated. And although a recrudescence of frank arthritis was not uncommon when salicylates were prematurely discontinued during signs of active disease, such an exacerbation was not observed among the rheumatic fever patients while adequate salicylization was maintained. Among those with rheumatoid disease, 91 per cent continued to show joint swelling for five weeks to several months, and in many cases there occurred an exacerbation or a progression of frank arthritis despite intensive salicylate therapy.

#### JOINT DEFORMITIES IN RHEUMATOID PATIENTS

Residual joint deformities, manifested chiefly by periarticular thickening, usually in the wrist, knee or ankle were observed in 63 per cent of the rheumatoid patients. In none of the patients with rheumatic fever could definite, residual joint deformity be demonstrated. Transient limitation of joint function and local muscle atrophy were occasionally seen in rheumatic fever convalescents. These were probably due to improper mobilization and were easily corrected.

Chorea and subcutaneous nodules are frequently mentioned in differential diagnosis, although they are rarely found in adult rheumatic fever. However, nodules should be sought for and biopsied, especially in the event of a diagnostic problem. The histologic picture may determine the rheumatic or rheumatoid nature of the disease.2 Nodules were recorded in two rheumatic fever patients, and in one rheumatoid. No case of chorea was observed in the presence of active carditis. Erythema in one or another of its many forms occurred in 7 per cent of the rheumatic fever group, while it was never observed in association with rheumatoid arthritis. The degree of fever, leukocytosis and/or anemia was not helpful in differential diagnosis. Signs of purpura, most commonly in the form of epistaxis, were observed in 22 per cent, while pulmonic changes occurred in association with rneumatic fever in 8 per cent of the cases. Only one patient with rheumatoid arthritis experienced spontaneous nose-bleeds, while neither pleurisy nor pneumonitis was ever observed.

A significant difference in the duration of the abnormally elevated sedimentation rates was noted. (Table2.) While the average period of high sedi-

Table 2.—Elevated Sedimentation Rates in Adult Rheumatic Fever and "Atypical" Rheumatoid Arthritis

Dura	tion	$\mathbf{RF}$	RA
Average		9.9 weeks	25.3 weeks
Elevated	1 - 4 weeks	33%	0
Elevated	5 - 8 weeks	28%	3%
Elevated	9 - 12 weeks	16%	17%
Elevated	13 - 24 weeks	16%	37%
Elevated	more than 24 weeks	7%	43%

mentation rates was approximately ten weeks among the rheumatic fever patients and 25 weeks among the rheumatoids, this contrast was even more striking when broken down further. Of the rheumatic fever group, 33 per cent showed a normal sedimentation rate four weeks after the onset of the disease; 61 per cent were normal within eight weeks. Of the rheumatoids, only one showed a normal sedimentation rate at the end of the eighth week, and the majority continued to have a high rate for several months thereafter.

It had been hoped that valuable aid in differential diagnosis might be derived from the antistreptolysin titer. The results were disappointing, chiefly because 60 per cent of the rheumatic fever group showed normal titers\* while as many as 22 per cent of the rheumatoids were abnormally high. Elevated antistreptolysin titers in acute rheumatoid arthritis have been previously described.

#### BONE AND JOINT X-RAYS

Bone and joint x-rays were normal among the rheumatic fever patients except for transient osteoporosis, which was observed in a few cases whose course had been marked by multiple recrudescences

<sup>\*</sup> It should be noted that the initial titers were not obtained before the sixth week of the disease in most cases.

of arthritis. The rheumatoid changes consisted chiefly of demineralization and joint narrowing. In this connection, it is well to remember that joint x-rays in rheumatoid arthritis may be entirely normal for months to years following the onset of the disease. Of great interest was the discovery that 39 per cent of the cases of rheumatoid disease showed significant changes in the sacro-iliac joints indicative of early rheumatoid spondylitis or socalled Marie-Strumpel disease. It has been recently shown that the spinal fluid protein in this type of case is often elevated. 10 Spinal fluid examination was done in seven such patients, of whom five showed normal values and two showed a protein concentration of 80 and 99 mg. per cent respectively. Spinal punctures performed on ten patients with rheumatic fever failed to show any increase in the spinal fluid protein. In the presence of symptoms and signs of rheumatoid spondylitis, an elevated spinal fluid protein may verify such a diagnosis despite the absence of positive x-ray findings and thereby assist in differential diagnosis.

The importance of carditis in the differential diagnosis of rheumatic fever and rheumatoid arthritis has been mentioned. However, neither the absence nor presence of cardiac involvement should necessarily determine the final diagnosis. It has been previously pointed out that carditis in adult rheumatic fever is not demonstrable in a significant percentage of cases. Occasionally one encounters carditis in association with rheumatoid arthritis. Often the two diseases coexist, either in the combination of rheumatoid arthritis and superimposed active rheumatic fever, or rheumatoid arthritis and inactive rheumatic heart disease. The latter was believed to be the case in four of the patients showing x-ray signs of rheumatoid arthritis. The proper differential diagnostic appraisal of such patients must rely to a great degree on the bahavior of the arthritis, as well as other clinical features.

It is said that differentiation between rheumatic fever without carditis and rheumatoid arthritis may be impossible. However, this should apply chiefly to those cases in which the joint manifestations subside in a few days. In such examples of atypical rheumatoid arthritis one cannot make an early unequivocal diagnosis. This must await prolonged follow-up studies. But in many cases of atypical rheumatoid arthritis an early, positive diagnosis can be made. On the basis of observations already recorded in this paper, the differential points listed in Table 3 should be most helpful toward this end. The following features are emphasized:

- 1. Carditis, when present, usually indicates rheumatic fever although not necessarily so.
- 2. The arthritis of atypical rheumatoid disease is apt to be progressive and not migratory, while in adult rheumatic fever it may be either progressive or migratory.
- 3. The progression of the arthritis may be slower in rheumatoid disease than in rheumatic fever.
- 4. Unlike rheumatic fever, the antecedent upper respiratory infection is infrequent in rheumatoid arthritis, and when it does occur the latent period is usually significantly shorter.

- 5. The therapeutic ineffectiveness of salicylates and their failure to halt further progression characterizes their action in rheumatoid arthritis. In rheumatic fever, the objective joint improvement is dramatic with the proper administration of salicylates, which exert an equally effective prophylaxis against recrudescences of frank arthritis.
- 6. Erythema, purpura and signs of pulmonary or pleural involvement should favor the diagnosis of rheumatic fever.
- 7. The elevated sedimentation rate of rheumatoid arthritis continues for a prolonged period, while in most cases of rheumatic fever it is of comparatively short duration.

With these points in mind, many if not all of the atypical rheumatoid arthritis cases which were mistakenly admitted into rheumatic fever centers might have been correctly diagnosed within a few weeks or days rather than months following the onset of the disease.

TABLE 3.-Most Helpful Differential Diagnostic Features

	Adult RF	"Atypical" RA
Carditis	Often present.	Usually absent.
Arthritis	Progressive or mi- gratory, faster in its evolution; no objective residue.	sive, slower in its
Antecedent URI	Usually present with longer latent period.	Usually absent; shorter latent period.
Effect of Salicylates	Prompt improve- ment of objective joint findings; pro- tects against joint recrudescences.	May be totally ineffective.
Erythema	Often present.	Not observed.
Purpura	Often present.	Rare.
Pleurisy	Often present.	Rare.
Pneumonitis	Often present.	Not observed.
Elevated Sed. Rate	Usually of shorter duration.	Usually over pro- longed period.

#### SUMMARY AND CONCLUSIONS

- 1. A comparative study was made of 252 soldiers with active rheumatic fever with carditis and 33 soldiers with acute, "atypical" rheumatoid arthritis with diagnostic joint and x-ray changes.
- 2. The most helpful differential diagnostic features have been outlined.
- 3. It is concluded that accurate and relatively early differentiation between adult rheumatic fever with or without carditis and atypical rheumatoid arthritis can be accomplished in a significant number of cases.

655 Sutter Street, San Francisco.

#### REFERENCES

- 1. Bauer, W.: The Diagnosis of the Various Arthritides, New England Journal of Medicine, 221:524 (Oct. 5), 1939.
- 2. Bennett, G. A., Zeller, J. W., and Bauer, W.: Subcutaneous Nodules of Rheumotoid Arthritis and Rheumatic Fever, Arch. of Path., 30:70 (July), 1940.
- 3. Comroe, B. I.: Arthritis, Philadelphia, Lea and Febiger, 1944.
- 4. Dawson, M. H.: Chronic Arthritis, Nelson's New Loose-Leaf Medicine, 605, 1935.

5. Dawson, M. H. and Olmstead, M.: Antistreptolysin Titers in Rheumatoid Arthritis, Proc. of Soc. for Exper. Biol. & Med., 34:82-84 (Feb.), 1936.

6. Engleman, E. P.: Adult Rheumatic Fever, Presented at American Rheumatism Association, New York City, June, 1946, to be published.

7. Fischer, A.: Rheumatismus and Grenzgebiete, Berlin, J. Springer, 1933.

8. Freund, E.: Gelenkerkrankungen, Berlin, Urban and Schwarzenberg, 1929.

9. Hench, P.: Chronic Arthritis, in Barr's Modern Med:cal Therapy in General Practice, 1940.

10. Ludwig, A. O., Short, C. L., and Bauer, W.: Rheumatoid Arthritis as a Cause of Increased Cerebrospinal-Fluid Protein, New England Journal of Medicine, 228:306 (March 11), 1943.

11. Master, A. M. and Jaffe, Harry: Rheumatoid Arthritis and Acute Rheumatic Fever—The Differential Diagnosis, J.A.M.A., 98:881 (March 12), 1932.

12. Swift, H. F.: Rheumatic Fever, American Journal of

Medical Sciences, 170:631 (Nov.), 1925.

## Public Measures for the Control of Rheumatic Fever in England

JOHN PARKINSON,\* M.D., F.R.C.P., London

DURING the 17th century rheumatism affecting the body and multiple joints was first distinguished from gout which had previously been confounded with it. In 1676 Thomas Sydenham gave the first full clinical description of acute rheumatism and said that it chiefly attacked young people. Some years later he also described chorea, which was for a long time called Sydenham's chorea. But it was not until about 1800 that it became recognized, thanks largely to David Pitcairn and Matthew Baillie, that rheumatism was a disease which commonly affected the heart. Then in France Corvisart in 1806 began to refer to carditis, and Bouillaud in 1835 to describe and stress the frequency of endocarditis in acute articular rheumatism. By 1845, a century ago, a big step was reached when Sir Thomas Watson could write in his textbook of Physic: "It is a curious circumstance that rheumatic carditis is sometimes the first step in the whole disease; the cardiac symptoms will sometimes, I mean, precede those of the joints; even by two or three days."

Towards the year 1890 the medical profession in England began to realize that in acute rheumatism (or rheumatic fever) the country was faced with a problem of great national importance as a common source of cardiac disease. The British Medical Association carried out a collective investigation not only into its clinical features but also into the distribution and social and environmental associations of the disease.

Cheadle, a London physician and pediatrician, published in 1889 his lectures entitled "The various manifestations of the rheumatic state," lectures in which he urged a wider view of rheumatism than that of a polyarthritis: that the carditis was the essential fact about it, and not the condition of the joints which might be minimal and was often overlooked. Public attention to the subject was drawn by Sir Arthur Newsholme who produced the first epidemiological survey, and by Sir George Newman with his report from the Ministry of Health-not forgetting the powerful appeals to the profession and to the authorities by Dr. F. J. Poynton. The first direct result of this aroused public opinion was the setting aside in 1926 by the London County Council (L.C.C.) of 60 beds at Carshalton to accommodate children under the age of 16 with rheumatic fever. At the same time the other features of a general scheme for controlling rheumatic fever among the children of London were initiated.

#### THE LONDON COUNTY COUNCIL RHEUMATIC SCHEME

It seems best to describe the London County Council Rheumatic Scheme of control as it was in operation in 1938-39, before the second world war broke out.

#### 1. The Source of the Rheumatic Cases:

There was already in operation by the L.C.C. a system of regular medical examination of all school children by school medical officers whose function was almost entirely diagnostic, and they became especially interested in the recognition of rheumatic manifestations among the children routinely examined. Then, general practitioners who in their practice found a child suffering in this way, were invited to communicate with the central office or supervisory center if the parents were willing for the child to be moved to hospital. These supervisory centers, to be described later, were also the source of many cases, chiefly relapses, among those already under their regular supervision. Lastly, most general hospitals, as well as children's hospitals in and around London, were glad to free their beds of some children with rheumatic infection who needed longer hospital treatment than they could continue to give.

It became apparent that an intermediate examination by a medical referee was necessary between the application for admission to hospital and the

<sup>\*</sup> Physician to the Cardiac Department of the London Hospital; Physician to the National Heart Hospital: Consulting Cardiologist to the Royal Air Force.

actual acceptance and transfer as a suitable case. The referee was usually a physician in charge of a local supervisory center and often he (or she) was on the staff of a hospital in the neighborhood. It was the referee's place to exclude children with cardiac failure added to carditis, and such were transferred to a general or children's hospital in London itself. The other reasons for exclusion might be evidence of a congenital and not of a rheumatic heart affection, incidental murmurs in another kind of general infection, and so on, outside the rheumatic province. The form of application having been accepted at the central bureau, and the patient approved by the medical referee, the child was then transferred by ambulance 20 miles to Carshalton or one of the other similar though smaller institutions in the country.

This short account clearly applies to London only, and it must be admitted that there has been evolved a most comprehensive scheme. Some other cities, however, have provided similar schemes including hospital schools. Bristol, for instance, will be remembered in this direction and largely because of the pioneer work of the late Dr. Carey Coombs.

#### 2. Institutional Treatment:

At Queen Mary's Hospital, Carshalton, the hospital school now provided many more beds, and with other smaller centers, the available beds provided by the L.C.C. numbered 900 in 1938. In addition, the hospital school at West Wickham early established by a voluntary organization—the Invalid Children's Aid Association—had grown until it provided for a further 100 children, making accommodation for 1,000 in all.

These institutions are more than convalescent homes and the name Hospital School describes them best. They have country surroundings with large open air terraces alongside the wards on to which the beds can be easily run; and it is the custom to carry out what is in fact open-air treatment, except in the most severe cases. Experienced medical officers have formed the opinion that if the children are warmly clad there is no additional risk of infection or chill, that appetite is quickened and sleep is sounder at night.

In severe carditis great stress is laid on complete immobility so that ample nursing facilities are essential. As grades of convalescence are reached, so movement is less restricted until later there are few restrictions and the children play in the grounds. From the beginning of convalesence, the teachers appointed by the Ministry of Education give daily lessons and school rooms are provided for those sufficiently recovered. The teachers live not far from the hospital. The education of rheumatic children is of great ultimate importance apart from the fact that the lessons pass the time so agreeably. It is to be remembered that eventually they should be fitted for some kind of sedentary work and, for this, education is at least as important as in healthy children. Moreover, proper pride in feeling trained for normal employment

would later enable a child to extricate himself more easily from the invalidism apt to accompany and follow the active disease. It is inseparable from the special purpose of these hospital schools that there must be a long stay in hospital, often weeks or months in bed followed by a prolonged convalescence under supervision. The usual length of stay is from six to twelve months.

#### 3. Supervisory Centers:

These were 20 in number and formed an integral part of the plan. They were distributed through London including the most thickly populated areas, and ten of them were organized at the out-patient departments of large hospitals. If no suitable accommodation existed at a hospital nearby, a house or building was adapted for the purpose and a special staff was appointed by the L.C.C. The medical officer in charge, usually of consultant status, was in control year after year. A nurse and a social worker were in attendance, and an almoner was deputed to visit the patients' homes and make their observations upon them. The purpose of these centers can be enumerated as periodical supervision especially of patients discharged from the hospital schools, diagnosis in cases referred to the center. instruction in child welfare to the parents of the children, and of others in the neighborhood. Simple pamphlets were distributed, and personal advice was given and passed on to the schools.

The important decision was taken whether the child should be educated at a physically defective (P.D.) school with its advantage of special control and ambulance transfer to and from school, or at an ordinary school with ampler opportunity for exercise. In either case liaison was established with the school medical officer.

The center was not intended for treatment, but it arranged where necessary for treatment at an out-patient department of a general or a children's hospital, unless of course a recurrence required the return of the child to the hospital school. After school age, young people with permanent valvular affections were transferred to an ordinary hospital out-patient clinic. Suitable employment was arranged by voluntary health societies such as the After-Care Association.

#### 4. Central Organization:

The central bureau was situated at the L.C.C. Headquarters on the Thames. There the whole scheme was controlled by the Supervising Medical Officer. He was responsible for the rheumatism register of medical records and for a card index of all the rheumatic children, past and present. who had been accepted at any center or hospital school. In 1938 this registered 22,800 children up to the age of 15 in London who were suffering or had suffered from rheumatic infection. It represented an incidence of about 2.6 per cent of the child population.

It may be noticed that I have made no mention of official reporting or notification of acute rheumatism. This was never adopted as part of the plan, except in an experimental way. In three London Boroughs and in certain provincial cities it was made officially notifiable, and the experience gained thereby is likely to be of interest now that the question of universal notification must come under consideration.

#### THE WAR PERIOD

When war began in 1939, there was a steady exodus of children of school age from London and other big cities which reached a stage almost of compulsion when bombing became a matter of fact, and not simply of its anticipation prompting precautionary measures. It was hoped that the hospital schools might be maintained, but as time went on and the bombing area extended, they had to be vacated. Children remaining at the largest hospital home, Carshalton, were transferred with others to a special hospital in the North of England.

When the war ended and children were once again seen in the streets of London, the L.C.C. and the school authorities were at first under great difficulties because of the distressed home conditions and the reduction by bombing of the schools available. Further, many teachers had not returned from the war. Medical officers were similarly slow in returning, but gradually there has begun a revival of the system of recognition and control of rheumatic fever as outlined above.

#### PLANNING FOR THE FUTURE

The passing of the New Health Act will have a profound effect upon the future solving of the problem of rheumatic fever. The whole of the health services and all the hospitals in the country will come under the control of the Ministry of Health in 1948, and 14 regions have been demarcated. They will be administered by Regional Councils each working as far as possible from a main University Center. Teaching hospitals retain more autonomy than others. Already the significance of this great change in the medical services of the country has been viewed from the standpoint of rheumatic fever.

Last year the President, warmly supported by the Royal College of Physicians, brought into existence a Rheumatic Fever Committee upon which are represented not only the College, but also the Ministry of Health, the University of London, the Medical Research Council, the London County Council, with cardiologists and pediatricians concerned in the problem. This body is at present concerned in the problem. This body is at present concerned in the will take the initiative in planning for a resumption of schemes like the L.C.C. scheme, not only in London but in each of the regions into which the whole country has now been divided.

#### REPORTING (OR NOTIFICATION)

There are some who think that reporting should be in the forefront of any campaign against rheumatic fever because if a large number of cases is reported it will rouse public opinion and strengthen

the demand for larger facilities. Most authorities, while agreeing that it is an essential, regard it as unlikely to succeed unless at the same time the whole scheme can be planned and set in motion. This may imply delay in issuing an order for compulsory reporting which should wait at least until there is hospital accommodation commensurate with the estimated total of reported cases. This is not a disease that can be left to swell a long waiting list! Meanwhile reporting may be applied to certain areas, as it has been both in England and in the United States, to provide information on its advantages and difficulties. In England it may prove that the difficulties are lessened by the introduction of a National Health Service. We shall think, I trust, not of larger statistics, but of ampler provision for all cases notified. Compulsory not voluntary notification is ultimately a necessity for public health control of rheumatic fever.

It is true that the L.C.C. register fulfilled to some extent the purpose of notification or reporting as it is termed in the United States. But it did not affect the primary sources in daily medical practice, for it was left almost entirely to the personal interest and choice of the general practitioner to decide whether to avail himself of the facilities provided or not. The essential is to convince or satisfy him that adequate facilities exist and are in operation, and that his cooperation is necessary for early diagnosis not only of frank rheumatic fever. but also of the more difficult even doubtful rheumatic manifestations. It is only reasonable that such particular work should have proper remuneration, and that it should be supported by easy reference to a specialist consultant. He should be available to be called to the patient's home for verification of the diagnosis, and if this is confirmed as ground for action, to quicken the transfer direct by ambulance to the hospital school in the country.

#### HOSPITAL ACCOMMODATION

The provision of sufficient beds for long-term treatment of rheumatic children seems to be the most urgent, and the most difficult, of the problems facing those who champion this great cause. At least it is as important as the provision of more hospital beds for adults to meet the unsatisfied demands of the people—a need in the United States as in England. After careful planning must come vigorous action on the part of all Heart Associations and similar bodies or the object will never be achieved. Such action is now in progress in the United States, as I know, and we in England expect that the priority next to provision of homes will be the provision of more hospitals. These must include hospital schools for rheumatic children wherever there is need for them, and the need is great.

#### EDUCATION OF PERSONNEL, AND RESEARCH

The early recognition and the whole management of rheumatic fever call for a considerable increase in the number of those trained for this

special task. Some of the larger hospital schools will become natural centers for the training of medical men who are prepared to devote some years at least to this subject. The training of nurses is equally important. Postgraduate instruction will naturally find a place in these specialized institutions, and valuable experience will be gained.

It is fortunate that through the benevolence of the Canadian Red Cross Society we have an opportunity in England to make use of a large hospital at Taplow for the formation of such a center. It served Canadian troops during the war and it is ideally situated in the country. The Ministry of Health has agreed to found there a hospital school of 200 beds for rheumatic children which will become a main center for treatment and research, and where doctors, nurses, and auxiliary helpers can be trained in preparation for extension of modern rheumatic schemes in different parts of the country.

Summing up, my personal view is that the most important features of a sound scheme of national control would be: (1) early diagnosis of rheumatic fever and early transfer; (2) provision of ample beds in hospital schools; (3) supervision during school age and after; (4) training of personnel, and (5) research on rheumatic fever. Finally, we need scarcely be reminded that the success of all parts of these comprehensive plans depends more than anything upon personal feeling and determination. The history of public measures for the control of rheumatic fever is mainly a history of individuals fully persuaded of the need and quite determined to awaken the public, the medical profession, and the authorities to the importance of the problem-and to work hard at it themselves. If a similar spirit actuates those who participate in any branch of the scheme, it cannot fail in due course to accomplish its great purpose.

1. Devonshire Place, London, W.I.

### Rheumatic Fever Control Program in California

HAROLD ROSENBLUM, M.D., San Francisco

R HEUMATIC fever and rheumatic heart disease are the leading causes of death in the age group 5-15 years and account for 25 per cent of all deaths due to heart disease.

Although our knowledge in the prevention, in the pathogenesis and development, in the diagnosis and in the treatment of rheumatic fever and rheumatic heart disease is incomplete, it is considerable and it is growing. Enough knowledge and public health techniques are at present available so that an effective attack upon the problem can be made.

Programs for the control of rheumatic fever, to be effective and enduring, must be clinical in approach and must offer tangible evidence to physicians that immediate benefit in terms of prophylaxis, detection and treatment is forthcoming to their patients. This will occur when such a program is medically controlled. The most comprehensive plan now in existence is the "London County Council's Rheumatism Scheme" which is described in this issue of California Medicine by Dr. John Parkinson.

In England, progress has depended in large part upon the extensive hospital facilities available there for the long-term care of children with rheumatic fever and rheumatic heart disease. In California, the nucleus of a rheumatic fever control program has been established. Its beginning consisted in the formation of the California Heart Association (1926) the function of which was then and is now to arrange postgraduate education in heart disease for the physicians of this state. The interest of physicians and of the general public was stimulated by the rheumatic fever program (1941-1946) in Solano and Contra Costa counties.

This was supported by the State Department of Public Health with funds made available by the Children's Bureau, and it resulted in the detection of over 300 cases of rheumatic fever and rheumatic heart disease, with provision for hospital and convalescent care for many of them. Meanwhile, yearly symposia open to all physicians in this and neighboring states have been held in San Francisco, Los Angeles and San Diego under the sponsorship of community heart associations. These functions have been correlated by the California Heart Association and assisted by the medical schools and leading hospitals of the respective areas with teaching ward rounds, clinical demonstrations and lectures. Many notable authorities have been brought to California as guest speakers to participate in these symposia, including Drs. T. Duckett Jones, Paul D. White, Tinsley Harrison, Arthur de Graff, Maxwell Wintrobe, Samuel D. Levine, John Parkinson and Helen Taussig. Speakers have been provided for local medical societies, auxiliary professional groups (teachers, social workers and nurses), and for interested lay groups, often sponsored by the California Congress of Parents and Teachers. In addition, scientific programs for physicians are conducted by the membership of the California Heart Association in connection with the annual meetings of the California Medical Association.

## HEART DIVISION OF CALIFORNIA TUBERCULOSIS ASSOCIATION

In 1943, motivated by a common interest in securing adequate facilities in California communities for the control of heart disease, the Cali-

fornia Tuberculosis and Health Association joined forces with the California Heart Association in forming a Heart Division of the California Tuberculosis and Health Association. This Heart Division provides an opportunity for health education and community organization in the field of rheumatic fever and rheumatic heart disease, utilizing the type of medical leadership, skills, techniques, and financial resources which has been effective in the fight against tuberculosis. This type of affiliation now exists not only on the state level but also in San Francisco, Los Angeles and in some 15 other local associations throughout the state. It is supported by the sale of Christmas seals.

The heart divisions of the tuberculosis associations have taken responsibility for: (1) the stimulation of interest in the development of sanitorial and hospital beds for rheumatic children; (2) the provision of educational material to parents, teachers and community leaders; (3) the support of legislative measures toward improvement in the care of crippled children; (4) assistance to local health departments in establishing necessary services; (5) assistance to local school departments in establishing health services, and, (6) integrating the activities of health and welfare services in the community.

The State Department of Public Health has helped to prepare communities for rheumatic fever programs by providing public health leadership, by lending the services of cardiologists, pediatricians and social workers in the organization of clinics and services, by providing training in the field of rheumatic fever to local physicians and, finally, by taking financial responsibility for the institutional treatment of rheumatic children not otherwise provided for.

In the development of a rheumatic fever program in a community, all the agencies mentioned above have participated. Often, a committee of leading physicians including the local health officer has met under the auspices of the local tuberculosis association, to discuss the rheumatic fever problem, the needs of the local community, the standards for a diagnostic clinic, and the required ancillary services. Authorities in rheumatic fever, cardiac disease and in public health have appeared before county medical societies, public health departments, school health departments, and teacher groups. Public interest has been invoked by health education programs through the Heart Division of the local tuberculosis association. The State Department of Public Health has provided consultation services in medical and other professional fields. Five local rheumatic fever detection clinics are now in progress. These are in Contra Costa, Sonoma, Kern and Santa Barbara counties and in the City of Pasadena. Humboldt and San Diego counties are about to embark on similar programs. Other counties in California are beginning the work of preparing for rheumatic fever clinics.

#### CASE REGISTRIES BEING DEVELOPED

Case registries for rheumatic children are being developed in San Francisco and Los Angeles counties. Although rheumatic fever and rheumatic heart disease are legally reportable in California, an adequate definition of the magnitude of the problem must await complete and effective reporting on a state-wide basis. Thus, the importance of accurate registration is obvious.

Our greatest shortcoming in the program for the care of the rheumatic child in California today is the lack of hospital and convalescent facilities. Of course, this is not peculiar to the rheumatic fever problem. We must admit, however, that the overall significance of this problem, its probable amenability to control and the benefits to be derived from early diagnosis and adequate treatment, make the provision for the extension of needed facilities of paramount importance. Medical thinking and community planning are far in advance of therapeutic facilities. This, in a sense, is comparable to the tuberculosis picture in the early 1900's. The next steps are to provide beds and to make support for a rheumatic fever control program for California secure. This can be done only by legislative action which will provide funds to assist local communities when they have exhausted their own resources in developing programs and facilities. This has already been done for our children with cerebral paralysis.

On a state-wide basis, under medical leadership, and with the fullest cooperation among the various Heart Divisions, the California Heart Association and the State Department of Public Health, much has been done. More remains to be accomplished. Although the program is young and incomplete, it is already more comprehensive than any in other states. It is our hope that all Californians will join hands in strengthening all the means which have been and can be mustered to control childhood's greatest enemy, rheumatic fever.

450 Sutter Street, San Francisco.



## Diagnosis and Treatment of Arteriovenous Aneurysm in a Naval Hospital

G. ARNOLD STEVENS,† M.D., Beverly Hills

BNORMAL communications between arteries and veins resulting from combat injury constitute a relatively infrequent but important prob-lem in a Naval Hospital. The vessels of the extremities are the most frequent sites of traumatic arteriovenous aneurysm, although the large vessels of the neck, the sub-clavian region, and the aorta and vena cava may be involved. The viability of the affected limb and, at times, the life of the patient, depend on correct diagnosis and proper treatment of the lesion.

#### DIAGNOSIS

The diagnosis is not difficult and is contingent upon an adequate appraisal of local and systemic

symptoms and findings.

Local Symptoms and Findings are definite and easy to elicit. There is a scar at the site of injury. Within a few months or less, compensatory enlargement of the involved limb is apparent. There is increased temperature of the involved area. The veins of the involved extremities become dilated. A bruit may be heard at the site of the arteriovenous communication. There is a pulsating expansile mass at the site of the fistula, and a thrill may be palpated. Pressure over the site of the fistula causes the thrill and bruit to disappear and results in a slowing of the pulse rate. The tributary veins to the fistula show a higher oxygen content than in other veins and conversely the regional arterial blood has a diminished oxygen content. Enlarged communications, pigmentation, ulceration, hemorrhage, and even gangrene of the extremity distal to the fistula may occur. Pain is an inconstant symptom. It is merely the result of pressure on nerves by larger fistulas.

Systemic Manifestations, although less obvious, are significant. Fall in blood pressure is an early effect. This results from an immediate decrease in the cardiac output, of peripheral capillary resistance and of the total volume of circulating blood. These early effects are identical to those resulting from any massive hemorrhage. Subsequently, compensatory reactions are evident. There is an increased rate of cardiac contractions with a resultant increase in the pulse rate, and increased filling of the right heart, and, therefore, increased output. The total blood volume is increased. The amount of the increase obviously is proportionate to the size of the arteriovenous fistula, as it is a compensatory phenomenon. Other factors influencing the cardiovascular dilatation are the duration

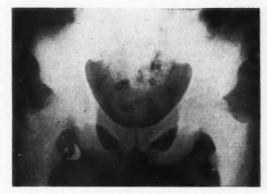


Figure 1.—Fragments of shrapnel causing femoral arteriovenous fistula.

of the fistula and its location in the arterial tree. The more proximal the fistula is to the heart, the greater the dilatation. Collateral circulation is stimulated and increases with time.

#### SURGICAL MANAGEMENT

The immediate treatment of the initial wound and site is within the province of the surgeon in the field of combat. The treatment is essentially that of hemorrhage, infection, and gangrene. The responsibility of the surgeon in the Naval Hospital resolves itself to the definitive care of the arteriovenous aneurysm. This report is concerned with this phase of the treatment.

Contrary to our previous conception, experience has shown that these cases may be operated upon safely within one to three months after the initial injury. In patients of the age group involved in the military service, adequate collateral circulation with the aid of compression will usually develop within this time. We have observed cases in which compression could not be tolerated for more than three minutes without distress in the involved extremity. These cases have, without exception, been able to tolerate 30 minutes' compression, twice daily, at the end of 30 days without pain. We have had no untoward experience following surgery when this routine has been followed. It is, of course, necessary to delay operation until edema, infection and local hematoma have subsided.

A number of operative procedures have been carried out in the treatment of arteriovenous fistula. Closure of the fistula with restoration of the artery and vein carries considerable risk and is only rarely possible. Preservation of the artery and vein with repair of the fistula in the artery wall sacrificing the vein, is too frequently attended by embolism and arterial aneurysm. Ligation of

Note: The opinions and views set forth in this article are those of the writer and are not to be considered as reflecting the policy of the Navy Department.

† Associate Clinical Professor of Surgery, College of Medical Evangelists; Consultant in Surgery, Veterans' Hospital, Los Angeles (Sawtelle).

the communication of the canal is rarely possible. Ligation of the artery and vein proximal to the fistula is a compromise and not a cure. Ligation of the proximal and distal artery is followed by a high percentage of recurrences as collaterals reestablish the communication. Ligation of the proximal artery alone is contraindicated because of the high rate of gangrene and ischemia. Ligation of the proximal vein alone may be used as a palliative life-saving procedure in cases of cardiac decompensation incident to arteriovenous fistula. It is not a cure. Closure of the fistula by triple ligation and twisting of the proximal vein may be used in high carotid arteriovenous fistulae. Quadruple ligation without excision and endoaneurysmorrhaphy is usually successful if all incoming branches are ligated.

The operation of choice, we believe, is quadruple ligation with excision of the arteriovenous fistula. If the artery and vein proximal and distal to the fistula are exposed and fixed with unbilical tapes before resection of the aneurysm is carried out, danger of serious hemorrhage is precluded. We recommend daily compression of the fistula beginning with three minutes and working up to 30 minutes twice daily. This can usually be accomplished without distress within 30 days. We realize that this procedure is possibly unnecessary in young individuals with adequate collateral circulation. However, the cases in which we have followed this procedure have not required sympathectomy to insure the viability of the limb. We therefore consider it a wise precaution. Chart.I reports six consecutive cases treated by this method with



Figure 3.—Resected femoral arteriovenous fistula with false aneurysms.

entirely satisfactory results. Figures 1, 2, 3, 4 and 5 are taken from this series of cases.

### PHYSIOLOGIC EFFECTS FOLLOWING RESECTION OF

The immediate effects of obliteration of the fistula are: a transient rise in general blood pressure followed almost immediately, by a fall to a lower level, a marked immediate slowing of the pulse rate, a decrease in venous pressure proximal to the fistula, and a marked decrease in cardiac output. The remote and permanent accomplishments are: gradual readjustment in the general blood pressure with decreased pulse pressure, a decrease in the total blood volume, a recovery to a normal pulse rate, and subsidence of dilatation of the heart and of the proximal artery and vein. In

CHART I

Case	Sex	Age	Location of Fistula	Operation	Result
1	Male	21	Left posterior tibial	Quadruple ligation and resection	Good
2	4.4	32	Left popliteal	41	**
3	44	20	Right femoral	44	6.6
4	44	24	Right femoral	44	44
5	66	23	Right femoral	46	6.6
G	66	19	Left brachial	**	4.4

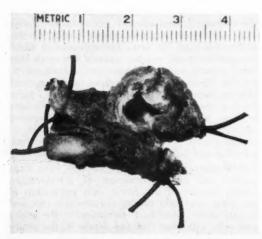


Figure 2.—Resected, arteriovenous fistula of femoral artery and vein with false aneurysm.

other words, the cause of the manifestations of over compensation, namely, the arteriovenous aneurysm has been eliminated.

#### CONCLUSIONS

- . 1. Six cases of traumatic arteriovenous aneurysm treated by quadruple ligation and resection with good results are reported.
- 2. Sympathectomy was not necessary in cases in which the fistula was compressed daily for 30 days before surgery to give added stimulus to collateral circulation. This procedure seems to be a well-advised precaution.
- 3. Resection of the fistula should be carried out three months or less after the initial injury. This minimizes such untoward compensatory manifestations as marked cardiac enlargement and deforming hypertrophy of the affected extremity.

120 South Lasky Drive, Beverly Hills, California.

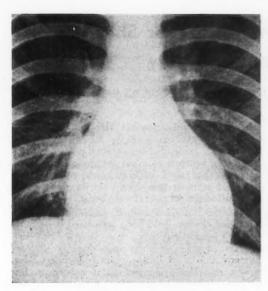


Figure 4.—Cardiac enlargement incident to femoral arteriovenous fistula.

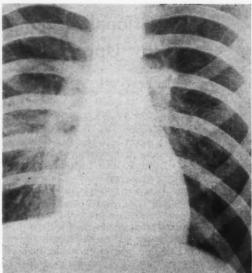


Figure 5.—Subsidence of cardiac enlargement following resection of arteriovenous fistula—same case as in figure 4.



76th Annual Session

California Medical Association

Los Angeles

April 30—May 3, 1947

## Fractional Spinal Anesthesia For Short Upper Abdominal Surgery

JOSEPH BRILL, M.D., Inglewood, AND D. E. STEWART, M.D., Huntington Park

EMMON'S method of spinal anesthesia has been variously called continuous or fractional, depending upon which aspect is emphasized. The continuous feature permits prolongation of anesthesia for long periods of time. The fractional feature enables the breaking of dosage to avoid large doses at any one time. It is the latter feature which is to be emphasized here in regard to high spinal anesthesia.

By a high spinal is meant the anesthetic in use for surgery of the upper abdomen. There has been more discussion of this type of anesthetic than of the less dangerous lower abdominal anesthetics. Credit must be given to Sise, Hand and Eversole for the glucose method of localizing the anesthetic agent against upward spread. However, they do not deny the dangers inherent in this method. The purpose of this discussion is to suggest the use of the fractional method for this type of surgery in an effort to develop control over the high spinal and thus eliminate some of the risk.

In general anesthesia, warning signals of overdosage are abundant, well understood, and time is available for stopping of further administration of the anesthetic agent before further damage is done. On the other hand, in spinal anesthesia the dose. once given, is irreversible and the reaction that occurs may be almost instantaneous. It is therefore logical to seek a method of divided spinal doses. It is most urgently needed in upper abdominal surgery because the area of cord anesthetized is a so the area from which respiratory and vasomotor nerves arise.

Therefore, it would seem safer to begin such an anesthetic with a minimal dose of 100 mg. novocaine or its equivalent, and add to it only when and if the condition of the patient warrants and if anesthesia is insufficient. Thus we escape the unpleasant dilemma of either giving one large, possibly dangerous, dose, or running the possibility of a failure of anesthesia and a switch to some other form of anesthetic.

That the minimal dose of 100 mg. of novocaine will often give sufficient anesthesia for upper abdominal surgery is known, as many of us have observed the anesthesia creeping up to the costal margin during a pelvic operation, and cholecystectomies have been performed without additional anesthetic on erroneously diagnosed appendicitis cases. Of course this dosage will not be sufficient in all cases, and the fractional method allows the addition of 50 or 75 mg. doses as needed.

It has been found in using the fractional method in upper abdominal surgery that fewer reactions occur. We use it in gallbladder and spleen surgery as well as in the more commonly indicated stomach surgery. The only possible risk in the method might be in the hands of the inexperienced who might fail to remember the cardinal purpose of this anesthetic, which is to avoid overdosage. The fractional method does require considerable experience and dexterity and should not be considered a method for the occasional anesthetist.

With the fractional method, relaxation has been good and closures have been facilitated. Originally we used the method only for prolonged cases such as gastrectomies or abdominoperineal resections, but now it is used with advantage in gallbladder, spleen, and less prolonged stomach surgery. Experience has given grounds for suggesting this additional indication for the fractional method.

The malleable needle technique is used. The syringe usually contains 200 mg. novocaine, and 20 mg. pontocaine, dissolved in 10 cc. isotonic saline solution. This is a 4 per cent solution, considering pontocaine as ten times the strength of novocaine. Ephedrine, 48.6 mg. (¾ grains) is used one half hour before surgery and repeated at the time of giving the spinal agent. The original dose is two and a half cubic centimeters, equaling 100 mg. of novocaine or its equivalent. Slight barbitoge may be used. There have been no complete failures of anesthesia, and in the few cases in which there was partial failure, switch was easily made to gas anesthesia (cyclopropane usually) or pentothal.

#### CONCLUSION

- 1. Increased controllability of high spinal anesthesia is desirable in order to gain added safety.
- 2. The fractional method offers increased controllability.
- 3. The fractional method is indicated in gallbladder and other upper abdominal surgery, regardless of the time duration factor.

#### CASE REPORTS

Case 1-Mr. J. M., 3942 St. Francis Hospital. Cholecystectomy. Age 49, weight 185 pounds. History of pain in the right upper quadrant for one year, unrelieved by medication. The patient had had a herniorrhaphy in 1944 under spinal and developed postoperative pneumonia. There was no such complication in this surgery which was performed under fractional spinal. The initial dose was 8 mg. of pontocaine in glucose. This first dose was given in a separate syringe in order to use a different drug for induction of anesthesia than for its continuation. A second syringe contained the additional dosage of 100 mg. novocaine and 10 mg. pontocaine in normal saline to equal 5 cc. This is a 4 per cent solution. The original dose was adequate until closure when 1 cc. (40 mg.) was added, giving good relaxation. Pentothal 1.0 gram was given for discomfort during traction. Time was one hour and forty-five minutes. The blood pressure began at 120/80 and rose to 140/80

where it remained throughout. The patient was dismissed ten days after the operation.

Case 2—Mrs. H. C., age 48; 4536 St. Francis Hospital. Common duct exploration. History of upper abdominal pain unrelieved by previous cholecystectomy. Surgery was performed under fractional spinal. The original dose was novocaine 100 mg. and pontocaine 2 mg. The exploration was thorough and surgery lasted three hours. Later additions of anesthetic totaled 200 mg. of novocaine-pontocaine solution, and pentothal, ¾ gram, was used to relieve discomfort during traction.

This patient remained in good condition throughout. Her blood pressure at the beginning of surgery was 140/90 and dropped only to 130/80. There was no dyspnea or cyanosis. She remained in the hospital till the twelfth day for the purpose of obtaining x-rays, and has had relief from her symptoms since the surgery.

Case 3—Mrs. E. N., age 51; 4848 St. Francis Hospital. Exploration and colostomy. History of intestinal obstruction and abdominal pain. Surgery was performed under fractional spinal. Initial dose was novocaine 100 mg. and pontocaine 3 mg. Duration two hours and fifteen minutes. Additional dosage of 75 mg. novocaine-pontocaine. In this case, instead of the suspected carcinoma, endometriosis was found which so narrowed the bowel lumen that a colostomy was necessary. The patient's condition was good throughout. Her blood pressure at the beginning of surgery was 120/80. It dropped to 105/70, but quickly rose to 140/90. She was dismissed from the hospital on the eighth postoperative day.

Case 4—Miss A. R., age 20; 15022 French Hospital. Purpura Hemorrhagica. Splenectomy was performed under fractional spinal. Initial dose was 110 mg. novocaine-pontocaine. Anesthesia was satisfactory for opening abdomen. Then insufficient relaxation was encountered, and no response was obtained by additional injections of spinal anesthetic. The malleable needle had become displaced and required adjustment to obtain a flow-back. However, in order to avoid delay, a light plane of cyclo-propone anesthesia was begun. Anesthesia was then satisfactory and the patient's condition remained good throughout. Bleeding was heavy, and two blood transfusions were administered, one in surgery and the other (500 cc. each) in the room. The blood pressure was entirely satisfactory, remaining at 120/80 throughout the surgery. The patient was dismissed 15 days after the operation.

Case 5—Mrs. F. M., age 38; French Hospital. Surgery was done under fractional spinal. The gallbladder region, including the entire abdomen was explored, with negative findings. The appendix was removed. The original dose of 120 mg. novocaine-pontocaine sufficed for this procedure, which lasted one hour. Convalescence was uneventful except for slight postspinal headache, and the patient was dismissed on the tenth postoperative day.

#### REFERENCES

Eversole, U. H.: Why Use Spinal Anesthesia? J.A.M.A., 128:256-261 (May 26), 1945.

Hand, L. V.: Spinal Anesthesia by Fractional Method of Administration, Anesth. & Analg., 21:189 (July-August), 1942.

Lemmon, W. F.: Method for Continuous Spinal Anesthesia, Ann. Surg., 111:141-144 (Jan.), 1940.

Cy

76th Annual Session

California Medical Association

Los Angeles

April 30—May 3, 1947

## Poison Oak - New Antigens and Their Effect On Sensitized Patients

ERNEST K. STRATTON, † M.D., San Francisco

THREE new poison oak antigens, designated as Antigens No. 95, No. 62 and No. 12 respectively, and prepared according to methods described in a previous paper,2 were administered to patients in order to compare their prophylactic as well as their therapeutic action. They were used both orally and parenterally. The oral administration was used to study their prophylactic affects, while both affects were studied when the antigens were given parenterally.

Patch testing with a standardized skin testing solution both before and after treatments was one of the methods used to determine the amount of immunity developing following the use of the three antigens. Technic: .01 cc. was applied to the flexor surface of the forearms under patch (Elastopatch, Duke). The patch was removed in 24 hours and the reactions read in 48 or 72 hours. The reactions were recorded as follows: negative; one plus (erythema, mild); two plus (erythema, more intense); three plus (erythema, intense, and with some edema); four plus (erythema, intense, with edema and vesiculation).

Antigen No. 95 (containing lobinol, the vesicant fraction) proved to be efficient when given orally but was much less so when given parenterally. (This finding is in agreement with Shelmire's experience with potent poison ivy antigens.

Antigen No. 62 (containing all of the fractions excepting the vesicant) was quite efficient when given parenterally but much less so when given by

Antigen No. 12 (containing the water soluble fraction) was of some value when injected but had practically no effect when given by mouth.

PROPHYLACTIC EFFECTS OF THE ANTIGENS

By Mouth: Antigen No. 95 was incorporated into tablets, each tablet containing 2,500 Dermatitant Units;3 and into capsules, each capsule containing 5,000 Dermatitant Units. It was prepared in this manner so as to protect the mucous membranes of the mouth and esophagus from the irritating effects of the vesicant. Patients were given two tablets per day for one month, then two capsules per day for two months, without interruption, unless some untoward symptom appeared. Thirty days after the last dose, a second patch test was made. There was considerable improvement noted in the patch test readings in most of the patients receiving this antigen by mouth. While none of the patients so treated became negative to the patch test, most of the 4 plus and 3 plus patch tests were reduced to 2 plus and 1 plus reactions and many patients who previously had been very susceptible to poison oak dermatitis volunteered the statement that they enjoyed comparative immunity for the first time.

Some of the annoying symptoms experienced by patients while taking this antigen were (a) pruritus ani and pruritus valvae, (b) mild generalized pruritus and (c) edema of the eyelids. These symptoms rapidly subsided as soon as the treatment was stopped. A few days later the treatment could usually be resumed by beginning with one-half of the disturbing dose, then gradually increasing it until the course was completed.

Antigen No. 62 and Antigen No. 12 were also incorporated into tablets, each tablet containing one milligram of solids. Patients were given two tablets per day for three months. There was some reduction in the intensity of reactions to the patch tests in those patients receiving Antigen No. 62, but none in those who received Antigen No. 12.

By Intramuscular Injection: Preliminary tests with the three antigens, administered by this route to patients, clearly indicated that Antigen No. 95 was the least efficient of the three in reducing the patch test reactions, so the following prophylactic study was made using Antigen No. 62 and Antigen No. 12.

A boys' club in San Francisco which has a summer camp in Bonneville, Mendocino County, had such a poison oak problem each summer that the author was invited to immunize volunteers prior to their departure for camp in the summer of 1945. The summer camp enrollment consisted of 185 boys between the ages of 6 and 16. One hundred and four volunteered for the preliminary patch test. (The patch test solution used was not strong enough to cause a reaction in an individual who had never been exposed to poison oak contact, but it was of sufficient potency to elicit a reaction in skins which had been already sensitized.) Of the 104 who volunteered, 49 (47.1 per cent) gave a positive reaction of varying degrees and 55 (53.8 per cent) gave negative readings. (Table 1.)

The 49 poison oak sensitive boys were given prophylactic injections of 1 cc. of the antigen intramuscularly every fourth day for four injections. Twenty-three boys (46.9 per cent) received Antigen No. 62 in oil (1 cc. contained 10 mg. of solids) and 26 boys (53 per cent) received Antigen No. 12 (1 cc. contained 10 mg. of solids). An attempt was also made to divide equally the number of 1, 2, 3, and 4 plus reactions receiving each antigen. Results of the patch tests made before injection, ten days after the fourth injection and 35 days after the last injection are recorded in Table 2. Of the 49 boys receiving the prophylactic treatments, 13 (26.5 per cent) developed poison oak dermatitis. Five of these had received Antigen No. 62 and eight Antigen No. 12. The nurses at the camp stated that none of these 13 cases suffered the tor-

<sup>†</sup>Research Associate, the George Williams Hooper Foundation for Medical Research, University of Cali-fornia Medical Center, San Francisco. This paper is No. IV of a series. (References 2, 3 and 4.)

POISON OAK

menting itch that usually accompanies the acute eruption.

Contrasting these statistics with those of the 81 boys who were at the same camp and who were not patch tested or given prophylactic treatment and in whom 44 or 54.3 per cent developed poison oak dermatitis, one could easily be led to believe that these two antigens had been of real help in protecting an otherwise susceptible group.

#### THERAPEUTIC EFFECTS OF THE ANTIGENS

Unfortunately, the facilities at the boys' camp had not been organized, either in equipment or personnel, to study the comparative effects of these antigens on the cases of acute poison oak dermatitis which developed there during the summer.

The following observations are personal ones made on some 30 volunteers suffering with acute poison oak dermatitis which the author treated himself during the course of a few months.

By Intramuscular Injection: Antigen No. 95 (1 cc. contained 10,000 Dermatitant Units of Lobinol). This antigen, as well as several of the commercial antigens on the market at present, contains the vesicant as the active principle. Many of the patients suffering from acute poison oak dermatitis who received this antigen were made worse. Several physicians with whom I have discussed this subject have had similar experience with this type of antigen and many have stated that they have stopped using them altogether in the acute cases.

Antigen No. 62 in oil. I have seen no aggravation of the eruption during the acute attack when this antigen was used. In a few patients, however, slight edema of the eyelids occurred during the course of injections. In general the symptoms subsided more rapidly and the patients seemed to be more comfortable with this antigen.

Antigen No. 12. Neither have I seen any aggravation of the eruption during the acute attack when this antigen was used. Edema of the eyelids, when present, subsided more rapidly with this antigen than with the others. Otherwise, I could not see that its use shortened the duration of the attack or made the patients any more comfortable.

#### COMMENT

The behavior of these new poison oak antigens in humans was very similar to that which this writer observed in animals.2 The development of immunity following their administration was a definite but slow process in both instances and while they are of value when used as a prophylaxis against poison oak, their action, I believe, is not rapid enough to be of much value as a therapeutic agent during the acute attack. Antigen No. 62 seemed to be the better one of the three for parenteral use. In the group prophylactic study, it gave the best record for protection and in my limited therapeutic study, its use appeared to give patients some relief and to shorten the duration of the acute attack. I would recommend that therapeutic studies be continued, using the intramuscular injection route for both Antigen No. 62 and Antigen No. 12.

#### SUMMARY

1. Three new poison oak antigens were administered as a prophylaxis to patients sensitized to poison oak. One antigen was found to be more efficient when given orally, another more efficient when given parenterally.

2. The incidence of poison oak dermatitis in two groups of boys in a summer camp was studied and compared. One group had received the antigens by injection as a prophylaxis, the other group had received none.

The three antigens were also injected into patients during acute attacks of poison oak dermatitis. Their actions are discussed and compared.

TABLE 1.

185 Boys, Aged 6-16, Attending Summer Camp Where Poison Oak Growth Was Luxuriant Numb	Number Developing Poison Oak er Dermatitis	Percentage
Boys who were positive to the poison oak patch test and who received prophylactic treatment before exposure 49	13	26.5
Boys who were negative to the poison oak patch test before exsure	10	18.2
Boys who refused to take the poison oak patch test	44	54.3

The author wishes to acknowledge the invaluable assistance given by Mrs. Hal E. Parsons and Mrs. Charles C. Nemetz in the routine of patch testing, preparing the boys for injections and keeping accurate records during the period of prophylactic study.

#### REFERENCES

- Shelmire, Bedford: Contact Dermatitis from Vegetation, So. Med. Jour., 33:337-46 (April), 1940.
   Stratton, Ernest K.: Poison Oak—New Antigens and
- 2. Stratton, Ernest K.: Poison Oak—New Antigens and Their Effect on Sensitized Guinea Pigs, Calif. Med., 66:70-74 (Feb.), 1947.
- 3. Stratton, Ernest K.: Poison Oak and Poison Ivy— Dermatitant Units as a Standard Measure of Potency for Extracts from These Plants, Jour. Allergy, 11:591-99 (Sept.). 1940.
- 4. Stratton, Ernest K.: Poison Oak and Poison Ivy, Immunity Studies in Guinea Pigs, Calif. & West. Med., 54: 115 (March), 1941.

TABLE 2.

Treatment Consisted				ch Tes			ays A		ch Tes			Veeks		h Tes		Poiso	of n Oak natitis
	Total No.	1+	2+	3+	4+	Not Done			1+	2+	Not Done		+	1+	2+	Cases De	eveloped Group
Number Receiving Pro- phylactic Treatment	49	18	13	16	2	9	15	10	8	7	13	16	9	7	4	13	26.5%
Number Receiving Anti- gen No. 62	23	9	6	7	1	3	9	4	3	4	4	8	6	3	2	5	21.7%
Number Receiving Anti- gen No. 12	26	9	7	9	1	6	6	6	5	3	9	8	3	4	2	8	30.8%

## The Newer Drugs for Allergic Disorders and Their Place in the Histamin Theory\*

MILTON M. HARTMAN, M.D., San Francisco

A LTHOUGH it has long been known that allergic phenomena are initiated by the union of antigens and their specific antibodies, the intermediary steps between this union and the manifestations of clinical and experimental allergy have been obscure. Such theories as (a) "disturbed colloidal equilibrium of the cell membranes and blood with serum flocculation," (b) "disturbance of the sympathetic-parasympathetic balance of the autonomic nervous system," (c) the "antigen-antibody combination acting as a specific toxin," and (d) the "enzymic action of the combination on body proteins producing toxins," have each had more evidence against it than for it.

In recent years the "Histamine Theory" has come to the fore as the one with the most clinical and experimental evidence for it and the least against. To sum it up, the antigen-antibody union taking place on the cell surfaces causes cell damage and dissolution of cell proteins, with the liberation of an H-substance, presumably histamine, which causes the increased capillary permeability, stimulation of secretions and smooth-muscle spasm characteristic of allergic reactions. The histamine is produced through the abnormal decarboxylization of the amino-acid histidine resulting from the protein decomposition (Figure 1). Ordinarily the shock-organ, skin, nasal mucous membrane, bronchiolar mucosa and smooth muscle, etc., determines which clinical entity is produced, such as urticaria, hav fever, asthma, etc. respectively, but if overwhelming amounts of histamine are released in the circulation the allergic reactions may be generalized.

Not only has histamine been isolated in increased concentration during experimental anaphylactic <sup>13, 25</sup> shock and in clinical allergic conditions, <sup>47, 57, 61</sup> but it also has the following properties, <sup>26</sup> which the intermediary H-substance has been demonstrated to possess: It is stable to boiling with hydrochloric acid, is dialyzable, inactivated by incubation with histaminase or diamine oxidase, and inactivated by condensation with diazotized sulfanilic acid. It lowers the blood pressure of etherized atropinized cats, the contractile effect on the guinea pig intestine is inhibited by arginine (and other "antihistaminic" compounds), produces wheals in the human skin, and is found in highest concentration in the eosinophiles <sup>14</sup> (characteristic of allergic reactions).

Histamine alone cannot completely explain all of the manifestations of anaphylactic shock or clinical allergy.<sup>15, 26</sup> The incoagulability of the blood in anaphylactic reactions, for example, is a phenomenon which requires the liberation of heparin 46 or a similar substance. Eczema and Contact Dermatitis cannot be as plausibly explained as urticaria and angioneurotic edema. Irreversible phenomena such as in periarteritis nodosa are not as well explained as the more common reversible type. In short, the histamine theory is a useful but not perfect working concept.

#### COUNTERACTION OF THE EFFECTS OF HISTAMINE

The rational practice of allergy attempts to interfere with the antigen-antibody union or control its location through proper elimination and desensitization procedures based upon etiological diagnosis so that the histamine problem does not arise. When such measures are not possible, not desired by the patient, or the results from them imperfect, the problem must be met. Counteraction of histamine is in many respects synonymous with the symptomatic control of allergic disorders and has been attacked on six fronts by the laboratory and clinician:

- A. Decomposition of histamine with histaminase.
- B. The use of antagonizing sympathetomimetic amines.
- C. Partial neutralization with antispasmodics.
   D. Increasing intolerance to histamine by physiological adaption.
- E. Production of histamine-neutralizing antibodies by antigenic histamine complexes.
- F. The administration of chemical blockers or "competitors," so-called "antihistaminic drugs."

A. The administration of the enzyme histaminase, obtained from the intestinal mucosa and kidneys of hogs, with the intent of decomposing histamine (presumably by deaminization) as soon as it is formed has had more laboratory than clinical success. The difficulties encountered clinically are the necessity of fresh preparations and of continuous administration, since the enzyme is far more effective prophylactically than it is after clinical manifestations are under way. Clinical effectiveness of histaminase varies from fair in serum sickness that and urticaria to practically zero in asthma.

B. Sympathetomimetic amines of course counteract the parasympathetic stimulation of histamine (its cholinergic effect, if you will). Unfortunately their therapeutic indices are quite low. Epinephrine is the classical antagonist of this type both experimentally and clinically; its properties and uses are too well known to require recounting. Of the host of drugs belonging to this group, only Butanefrine (Ethyl-nor-epinephrine) parenterally <sup>41</sup> or by inhalation; <sup>42</sup> Ephedrine, Propadrine and Nethamine <sup>40</sup> orally; and Privine, <sup>32</sup> Ephedrine, Propadrine and

<sup>\*</sup> Presented by invitation before the Northern California Chapter of the American Pharmaceutical Association, October 23, 1946, and before the San Francisco County Medical Society, February 18, 1947.

Neosynephrine for intranasal use can be considered as useful additions to our therapeutic armamentarium. Each has some differences from epinephrine which can be used to clinical advantage. Butanefrine (Figure 1), for example, has the bronchodilator effect of epinephrine, with less of its central stimulation and none of its vasopressic effect. It is therefore useful in nervous people, small children, and in the presence of cardiovascular disease.41 Privine has the advantage of prolonged vasoconstriction, but also has the disadvantage 33 of prolonged "rebound vasodilation." The aliphatic compound Tuamine (2-aminoheptane) 59 deserves mention as a useful substitute vasoconstrictor for people unable to tolerate the usual aromatic amines previously mentioned.29

#### PARTIAL NEUTRALIZATION WITH ANTISPASMODICS

C. Antispasmodics such as the xanthine group, papaverine, trasentin, etc., can be classified only as partial antagonists to histamine. Smooth muscle spasm induced by histamine is prevented or relaxed by such compounds experimentally and clinically, but the other pharmacologic effects of histamine are more or less unaffected. However, Theophylline Ethylenediamine, better known as Aminophylline, is most effective in asthma, and the same cannot be said generally for the newer "antihistaminic" drugs.

D. Attempts have been made to increase the physiological tolerance to histamine by its subcutaneous or intravenous administration. It was hoped that by these means the threshold to histamine stimulation could be raised above the point at which amounts ordinarily produced would be effective. Histamine, however, is a drug difficult to control, being highly diffusible and effective in such high dilution that unusual care must be exercised. Flushing, headache, urticaria and asthma may be induced while trying to prevent or alleviate same. Two general methods are in use: The subcutaneous method employs gradually ascending doses of the acid phosphate, starting in the 1:100,-000 dilution and ending at 0.2 to 1.0 cc. of the 1:1.000. Dosage is then maintained at the level just short of producing symptoms. This has been notably successful in Horton's Histaminic Cephalalgia 45 and the primary-vasodilative type of migraine. Urticaria has shown some response, but this method has been distinctly disappointing in other allergic disorders. The intravenous method has been of aid only in migraine 11 and urticaria, and is usually used only in interims between attacks. 2.75 mg. of Histamine Acid Phosphate is diluted in 500 cc. of normal saline and given by intravenous drip over a four to eight hour period. Three or four treatments on alternate days are enough for semipermanent effect. Its proponents 11 claim tolerance is raised more effectively by the prolonged contact, but interruptions are often necessary during the actual treatment for the administration of ascorbic acid or small amounts of epinephrine intravenously, and antiacids orally for the gastric distress due to high acid secretion (peptic ulcer danger!?).

E. Histamine itself is not antigenic, but the pro-

duction of neutralizing antibodies specific for histamine by the injection of an antigenic histamine protein complex has been accomplished. Landsteiner showed that the diazotization of simple chemicals and coupling to proteins resulted in the formation of antigenic complexes whose specificity was determined by the hapten portion.49 Recently a method has been developed for the heightening and preserving of histamine antigenicity with simultaneous elimination of its usual toxic effects and the antigenicity of the associated protein. The first step was the despeciation of horse serum globulin by partial digestion with Taka-diastase at pH 3.8 followed by neutralization. 16 The resulting globulin produced no reaction in people known to be acutely allergic to horse serum and dander. Histamine was then combined with paranitrobenzoylchloride in chloroform and triethylamine. The resulting paranitrobenzoyl histamine was then reduced with ferrous sulfate and ammonia to yield para-aminobenzovl histamine, which was then diazotized and coupled with the despeciated globulin. The resulting Histamine-azoprotein contains no free histamine, and is able to stimulate the formation of histamine neutralizing antibodies without producing histamine reactions.35 Milton Cohen showed that these bodies were specific for the histamine, not the azo or protein portion of the complex, and that in certain patients histamine-azoprotein produced a capacity for very rapid histamine neutralization. 17 He also demonstrated an increased skin threshold to histamine administered by iontophoresis in histamine-azoprotein treated patients 17 and increased refractoriness to eserine stimulation. 18

#### INDICATIONS FOR HISTAMINE-AZOPROTEIN THERAPY

Clinically histamine-azoprotein has shown its greatest value in the treatment of urticaria, angioneurotic edema and so-called physical allergy. 19,63 Unthinking enthusaists have harmed its cause by thoughtless use. Histamine-azoprotein is intended as an adjuvant to treatment rather than the sole remedy, and it is in no way a substitute for proper elimination and desensitization procedures based upon etiological diagnosis. When desensitization treatment produces suboptimal results because some antigen-antibody combination still takes place on cell surfaces with the release of histamine, histamine-azoprotein therapy is properly indicated. It is also indicated when the allergen cannot be identified after the most careful search, or in conditions in which the available antigens are weak, unstable or ineffective. In flea-bite sensitivity, to give an example of the last group, histamine-azoprotein has scored a notable success. 43 Apparently the amount of potential histamine neutralization engendered is enough to make the difference between comfort and misery.

F. The administration of chemical blockers or displacers is an old but fascinating subject in allergy, although to read the current newspapers and lay magazines one would infer that "antihistaminic" compounds were recent discoveries by completely altruistic drug companies.

Histamine antagonism is not necessarily synony-

mous with clinical relief, because histamine alone may not be the cause of the illness. Also, histamine has many physiological actions, and the compound under investigation may counteract only one or some but not others. Finally, the results of animal experimentation cannot be translated immediately into data for clinical use. In measuring antispasmodic action, for example, there are several pitfalls. Antispasmodics are of two general types:60 The Musculotropic ones such as the nitrites and papaverine are tested against Histamine Phosphate (2x10<sup>-6</sup> gm./cc.) and Barium Chloride (10-4 gm./cc.). The Neurotropic ones such as atropine and scopolamine are tested against acetylcholine bromide (10-6 gm./cc.). The more peripherally acting musculotropic group would be of most interest to the allergist even without the concept of histamine antagonism. What may be relatively more musculotropic in one species may be relatively more neurotropic in another, and vica versa.

Experimentally the simple amino acids Histidine, Cysteine, and Arginine will all inhibit histamine-induced contractions of the guinea pig intestine, 21 but the amounts required for clinical use would be toxic. For example, 2,500 or more parts of arginine are required to counteract 1 part of histamine. Ascorbic acid (Vitamin C) has the same action but the amounts required are large experimentally and ineffective clinically (except under special circumstances). Aminophylline and epinephrine, previously mentioned, also have this action, and from that standpoint could be considered as "antihistaminic" drugs.

The new "antihistaminic" drugs should more accurately be discussed under the heading of Dial-kylaminoalcohol compounds because of their essential chemical structure. Antihistaminic phenolic ethers of amino alcohols have been known since 1910, but were too toxic for clinical use. Procaine

(p-aminobenzoyl-diethylaminoethanol), which we are accustomed to regard only as a local anesthetic, is an antihistaminic drug particularly useful in serum sickness and urticaria. 1,65 Combinations of various aminoalcohols and chemical modifications of diphenylacetic acid have long been known to be antispasmodics. The aminoalcohol determines the nature of the action, while its intensity is modified by the acid group employed. If, for example, the diphenyl acetic acid ester of dimethylaminoethanol is prepared the result is a Neurotropic antispasmodic (Trasentin). If, on the other hand, the ester of 9.10-Dihydroanthracene-9-carboxylic acid is prepared the result is a Musculotropic one. Many of these compounds have more or less local anesthetic action, which appears to correlate more closely with musculotropic action than with other properties.50

The members of this recently publicized and growing family of "antihistaminics" of interest to us doing clinical allergy are Procaine, Benadryl, Pyribenzamine, Antergan, and Beta-dimethylaminoethyl 9,10-Dihydroanthracene-9-Carboxylate Hydrochloride, to be referred to hereafter as No. 887. Their structural formulae are shown in Figures 2 and 3.

Figure 1.

Diphenyl-Acetic Acid

Trasentin Beta-diethylaminoethyl 9,10-Dihydroanthracene-9-Carboxylate Hydrochloride

Figure 2.

Figure 3.

Note the dimethylamine-ethane or diethylamino-ethane group invariably present. All of them have local anesthetic action and secondary to that are cerebral depressants, a fact not sufficiently recognized. Their mode of action is a blocking one; 69 they combine with the site of action of histamine, occupying it primarily when given prophylactically or displacing it when given therapeutically. Histaminase is neither potentiated nor inactivated by their use and serum antibody levels are unaffected. Their absence of peripheral vasoconstrictor effect is evidence against a sympathomimetic effect. The release of histamine by antigen-antibody reaction is not prevented, and there is no evidence that the drugs combine with histamine itself.

Two standard methods adopted by laboratories in testing survival from ordinarily fatal histamine doses are: (a) the administration of a presumably protective dose of "antihistaminic" followed by histamine subcutaneously (or intravenously) and (b) a protective dose followed by histamine aerosol inhalation.<sup>52</sup> An examination of the comparative figures obtained by this last method would be of interest.

#### AEROSOLIZED HISTAMINE IN GUINEA PIGS

Dose in mg./kg. required to protect against asthma:

Needless to say, these figures are not directly transposable to the human. Other histamine induced phenomena have been studied with these drugs: inhibition of guinea pig intestine contractions; prevention of blood pressure drop in etherized atropinized cats; prevention of bronchoconstriction induced by lung perfusion; prevention of bronchoconstriction in barbitalized dogs intravenously induced; and prevention of vasodepressor effects of epinephrine. Decrease in gastric acidity

Figure 4.

and total secretion have been noted in animals and the human, <sup>55</sup> this effect being most marked with Benadryl. Except for Procaine, therapeutic indices are large and chronic toxicity studies thus far have been negative.

Procaine is the most familiar member, and, curiously enough, it is itself a fairly frequent cause of clinical allergy of the contact type. Its clinical use in allergy thus far has been limited to the treatment of serum sickness and urticaria. 1.65 One gram in 500 cc. normal saline is given intravenously over a two-hour period, and the treatment may be repeated daily. Of 16 cases of serum sickness, State 65 completely relieved ten and temporarily relieved four, and relieved six of seven cases of urticaria. In addition to "antihistaminic" action, one must consider the direct anesthetic action on the cells, decrease of acetylcholine liberated at terminals of efferent fibers, and epinephrine potentiating action.

For practical purposes, Benadryl and Pyribenzamine are clinically equivalent, 1 to 2 parts of either being required to counteract 1 part of histamine, depending on the circumstances. Because one has an ether linkage and the other a nitrogen linkage they are not exactly comparable pharmacologicaly. They are both effective orally, and clinical relief, when obtained, is evident in twenty to thirty minutes. Dosage varies from 50 to 500 mg. daily for an adult, the average effective plan being 50 mg. three or four times daily. The parenteral route is neither advisable nor ordinarily necessary, epinephrine being safer and more useful in emergencies, but Benadryl has been used in doses of 20 to 40 mg.

intravenously or intramuscularly. Benadryl is irritating in over 0.5 per cent concentration, so that its intranasal use is not advisable. Pyribenzamine has not been tried that way, but it seems inadvisable to use any local anesthetic intranasally for symptomatic relief.

It is difficult to give the percentages of various conditions in which relief may be expected from Benadryl or Pyribenzamine, because the reporting investigators varied in their dosages, in their definitions of the conditions treated, and in their criteria of relief. Here are reasonable "round-figure" averages compiled from over 2,600 cases\* in current medical literature. How much allowance has been made for the variability of allergic manifestations and spontaneous improvement is unknown.

The state of the s	
	5%
	5%
Dermographism	10%
	0%
Contact dermatitis (the pruritus only)	10%
Seasonal allergic rhinitis (hay fever)	0%
Perennial allergic rhinitis (extrinsic cause	0%
Vasomotor rhinitis-hyperesthetic rhinitis (intrinsic?)	
Seasonal asthma (associated with hay fever) 4	5%
Perennial asthma (extrinsic etiology demonstrated) \ 3	10%
Perennial asthma of unknown etiology (intrinsic?) {	
Asthma precipitated by acute (upper) respiratory infectionZer	0 %

The number of cases of migraine, histaminic cephalalgia, gastro-intestinal allergy, serum sickness, and pruritus of miscellaneous origin thus far treated do not permit of reliable conclusions; the statistically-minded may use 50 per cent, 60 per cent, 85 per cent (Benadryl)-28 per cent (Pyribenzamine), eighty per cent and sixty per cent, respectively, temporarily. Of the two drugs, only Benadryl has been used clinically to depress gastric secretory activity in gastro-intestinal conditions. 55

Maximum effectiveness is shown in the conditions exhibiting wheal formation, as might be expected. The perennial rhinitis and asthma cases include both those in which a definite allergic cause can be demonstrated and those of unknown origin. A clinical impression is that results in the latter group are much poorer than in the former. Asthma precipitated by acute respiratory infection is conspicuously unrelieved, and the result in asthma other than that associated with pollinosis are not spectacular. All of these figures include both total and partial relief; about one-third of those relieved are only partially so. All relief is purely temporary, the symptoms usually recurring promptly in the chronic cases on discontinuance of treatment.

We know of Antergen only from the reports of French investigators.<sup>5, 12, 24, 38</sup> The general properties are the same as those of Pyribenzamine, but four or five times larger doses are required clinically. The more recent Neoantergan is claimed to be more effective and less toxic than Antergan.<sup>7, 23</sup>

The side effects of these drugs are by no means minor, as they limit their clinical usefulness and necessitate certain precautions in directions and occasionally counteracting adjuvants (which are in themselves not innocuous). The most frequently occurring side-effects are sleepiness of varying de-

gree, nausea and vomiting, dizziness, headache, dry mouth, nervousness and gastro-intestinal cramps. Various authors have reported incidences of 20 per cent to 70 per cent of their series having side-effects. The majority, including the author, note about 50 per cent. Of these, one-tenth to one-half have to discontinue the drug, again the figures depending on the author's estimate of what is serious or dangerous. The order of reactions with Pyribenzamine is: Sleepiness, nausea, headache, gastro-intestinal cramps, dizziness, nervousness and dry mouth. The order with Benadryl is: sleepiness, dry mouth, nervousness, dizziness and weakness.

Whereas the hypnotic effect is a useful one at night, it is dangerous during the day and can be the cause of accidents. The first few doses should always be taken while a person is in a safe place under observation (not necessarily by a physician), and not while at work around such things as ladders, scaffoldings, machinery, etc. Counteracting these effects with caffeine or amphetamine stimulation may merely add the undesirable effects of these drugs, such as nervousness and loss of appetite. Sedatives must, of course, be used cautiously, and one must be doubly careful about the administration of anesthetics for emergency operations.

The indications for the use of Benadryl and Pyribenzamine may be summed up as follows:

- (a) The control of diffuse skin irritability and Dermographism so that the performance of specific skin tests is possible.
- specific skin tests is possible.
  (b) The control and prevention of testing and treatment reactions.
- (c) The maintenance of allergy patients in comfort for a few weeks until specific desensitization becomes effective.
- (d) The control of acute transient allergic manifestations.
- (e) The control of pruritus in general in order to minimize scratching and the attendant danger of infection.
- (f) The control of urticaria following sulfonamides, antibiotics,<sup>62</sup> organ extracts, serums and indispensable drugs.
- (g) Infrequently, the control of gastric acidity.

The possibility of acquired allergy to the drugs themselves is not fantastic, as urticaria from both has been noted. Anemia resulting from the anacidity is possible from long continued use, though how probable that is we do not yet know. The aromatic rings and coal tar origin suggest the possibility of agranulocytosis, and of caution in administration to salicylate-sensitive persons.

Beta-Diethylaminoethyl 9,10-Dihydroanthracene-9-Carboxylate Hydrochloride (No. 887) cannot yet receive a general comparison with Pyribenzamine and Benadryl, because it has been clinically evaluated only in asthma. Since the supply available was limited, it was tried only in this condition, in which Pyribenzamine and Benadryl were relatively ineffective. Experimentally it is about 20 times more potent than papaverine and about one-fifth as effective as epinephrine in relaxing spasm of the bronchioles induced by histamine. From the viewpoint of acute toxicity there is a wide margin

of safety, but the hypnotic action (also a local anesthetic!) is a limiting factor for daytime use. No adverse effects or habituation have been observed from prolonged administration. Oral administration to 90 cases of asthma of varying grades of severity provided 80 per cent of them with definite benefit, a marked contrast to Benadryl and Pyribenzamine. The optimum dose on retiring appears to be 200 mg., but during the day 100 mg. every four hours appears to be enough unless the asthma is quite severe.

By way of conclusion, some philosophy may be added to allergy. Up to 1932, 165 methods of inhibition of anaphylaxis had been described. In the last fifteen years there have probably been hundreds more. Out of all of these relatively few have proven their value. The successes have been characterized by prolonged preliminary investigation in ethical laboratories and clinical trial by objectivelyminded, conservative allergists. The possibilities inherent in the compounds could be predicted fairly well from their chemical structure and groupings. Conversely, unwarranted claims can often be shown up by a consideration of chemical structure, concentrations employed and methods of use.

The desire of newspapers to present information that is startling rather than factual has led to the recent unwarranted publicity for Anthallan, pur-portedly an "antihistaminic" drug, and Ethylene Disulphonate (Allergosil), not "antihistaminic" but unfortunately confused with them (Figure 4). Supposedly present in allergic individuals is a "defect in intracellular oxidation-reduction mechanisms and disordered carbohydrate breakdown." Ethylene disulphonate is the synthetic catalyst proposed to correct this regrettable defect.30 Small amounts in a dilution 1x10<sup>15</sup> in distilled water are administered intramuscularly. The temporary pain and muscular fibrillation observed are no doubt due to the practically pure water injected (and at what a price!) A few enthusiasts have published papers of questionable scientific worth, but the consensus of opinion 4,8,21 of recognized allergists is that the compound has no value and cannot be distinguished in its effects from distilled water.

Anthallan (Di (n-butyl) aminomethyl-trihydroxy benzofuranone) is purported to have antihistaminic effect pharmacologically, but it is as clinically inactive as its structural formula is unpromising. Ouestionable criteria of allergy were used in the conduct of the clinical investigations.28 In fact one investigator claims that "not only can hyperesthetic rhinitis [please define that term for us!] be treated simply and effectively with this drug, but the diagnostic problem can be ignored."39 With these noble words allergists are wafted from usefulness into obsolescence.

450 Sutter Street, San Francisco 8.

#### REFERENCES

- 1. Appelbaum, E., Abraham, A., and Sinton, W.: A Case of Serum Sickness Treated with Procaine Intravenously, J.A.M.A., 131:1274 (Aug. 17), 1946.
- 2. Arbesman, C. E., Koepf, G. F., and Lenzner, A. R.: Clinical Studies with Pyribenzamine, J. Allergy, 17:275 (Sept.), 1946.

- 3. Arbesman, C. E., Koepf, G. F., and Miller, G. E.: Some Antianaphylactic and Antihistaminic Properties of N'Pyridil, N'Benzyl, Dimethylethylenediamine Monohydro-
- chloride (Pyribenzamine), J. Allergy, 17:203 (July), 1946.
  4. Archibald, H. C.: Ethylene D.sulphonate and Sterile
- Distilled Water Controls in the Treatment of Children's Allergies, Arch. Pediat, 62:219, 1945.

  5. Aubertin, E.: Une Nouvelle Médication dans le Traitement des Maladies par Hypersensibilité: Les Antihistaminiques de Synthése, J. de Méd. de Bourdeaux, 119:606, 1042
- 6. Best, C. H. and McHenry, E. W.: The Inactivation of Histamine, J. Physiol., 70:349 (Dec. 4), 1930.
- 7. Bovet, D., Horclois, R., and Watthert, F.: Proprietes Antihistaminique de la N-p-methoxybenzyl-N-dimethylaminoethyl a Amino-pyridine, Compt. Rend. Soc. de Biol., 138:99, 1944.
- 8. Brenner, H. H. and Stoesser, A. V.: Ethylene Disulphonate in Chronic Asthma, Ann. Allergy, 4:179 (May-June), 1946.
- 9. Brown, E. A.: The Vitamins and Allergy, Ann. Allergy, 2:156 (March-April), 1944.
- 10. Burtner, R. R. and Cusic, J. W.: Antispasmodics. II—Basic Esters of Some Polynuclear Carboxylic Acids, J. Am. Chem. Soc., 65:1582, 1943.
- 11. Butler, S. and Thomas, W. A.: Intravenous Histamine in the Tretment of Migraine. Preliminary Observations, J.A.M.A., 128:173 (May 19), 1945.
- 12. Celice, J., Perrault, M., and Durel, P.: Utilisation Clinique des Antihistaminiques de Synthése, Bull. et Mém. Soc. Méd. d. Hôp. de Paris, 58:284, 1942.
- 13. Code, C. F.: The Histamine Content of the Blood of Guinea Pigs and Dogs During Anaphylactic Shock, Am. J. Physiol., 127:78 (Aug.), 1939.
- 14. Code, C. F. and MacDonald, A. D.: The Histamine-Like Activity of Blood, Lancet., 2:730, 1937.
- 15. Code, C. F.: The Mechanism of Anaphylactic and Allergic Reactions, Ann. Allergy, 2:457 (Nov.-Dec.), 1944.
- 16. Coghill, R. D., Fell, N., Creighton, M., and Brown, G.: The Elimination of Horse Serum Specificity from Antitoxins, J. Immunol., 39:207, 1940.
- 17. Cohen, M. B. and Friedman, H. J.: Antibodies to Histamine Induced in Human Beings by Histamine Conjugates, J. Allergy, 14:195, 1943.
- 18. Cohen, M. B. and Friedman, H. J.: Immunity Against H-Substance, J. Allergy, 15:245, 1944.
- 19. Cohen, M. B.: Urticaria and Angioneurotic Edema. A Summary of Our Present Knowledge, Ohio State M. J., 39:1120, 1943,
- 20. Committee on Pharmaceuticals and Medicaments of the American Academy of Allergy: A Report of the Clinical Studies on the Use of Pyribenzamine in Allergic Diseases, J. Allergy, 17:325 (Sept.), 1946.
- 21. Council Report: Ethylene Disulphonate, J.A.M.A., 131:1495 (Aug. 31), 1946. Editorial: Ethylene Disulphonate and Allergy, J.A.M.A., 131:1502 (Aug. 31), 1946.
- 22. Curtis, A. C. and Owens, B. B.: Benadryl in Treatment of Urticaria, Arch. Dermat. & Syph., 52:239, 1945.
- 23. Decourt, M. J.: La Medication Antihistaminique, La Semaine des Hospit. de Paris, 21:707, 1945.
- 24. Decourt, P.: Action de Bases Antagonistes de l'Histamine Sur Quelques Maladies Liées à des Réactions d'Hypersensibilité, Bull. et. Mém. Soc. Méd. d. Hôp. de Paris, 58:265, 1942.
- 25. Dragstedt, C. A. and Gebauer-Fuelnegg, E.: Studies in Anaphylaxis. I.—The Appearance of a Physiologically Active Substance During Anaphylactic Shock, Am. J. Physiol, 102:512, 1932.
- 26. Dragstedt, C. A.: The Significance of Histamine in Anaphylaxis, J. Allergy, 16:69 (March), 1945.
- 27. Edlbacher, S., Jucker, P., and Baur, H.: Die Beinflussung der Darmreaktion des Histamins Durch Aminosauren, Hoppe Seylers Ztschr. f. Physiol. Chem., 247:63,
- 28. Editorial: Anthallan and Rhinitis, J.A.M.A., 131: 745 (June 29), 1946.
- Engelsher, D. L.: Unusual Ephedrine Reaction, New York State J. Med., 45:307, 1945.

- 30. Evans, G., Bodman, J., and Maisin, J. H.: The Chemical Control of Allergy, Med. Press and Circular CCIII, May 29 and June 5, 1940.
- 31. Eyermann, C. H.: Clinical Experiences with a New Antihistaminic Drug (Benadryl), J. Allergy, 17:210 (July), 1946.
- 32. Fabricant, N. D. and Van Alyea, O. E.: A Note on the Evaluation of Privine Hydrochloride As a Nasal Vasoconstrictor, Am. J. Med. Sci., 205:122 (Jan.), 1943.
- 33. Feinberg, S. M. and Friedlaender, S.: Nasal Congestion from Frequent Use of Privine Hydrochloride, J.A.M.A., 128:1095 (Aug. 11), 1945.
- 34. Feinberg, S. M. and Friedlaender, S.: Relief of Dermographism and Other Urticarias of Histamine Origin by a Synthetic Benzhydryl Alkamine Ether, J. Allergy, 16:296 (Nov.), 1945.
- 35. Fell, N., Rodney, G., and Marshall, D. E.: Histamine-Protein Complexes; Synthesis and Immunologic Investigation. I.—Histamine-Azoprotein, J. Immunol., 47:237, 1943.
- 36. Foshay, L. and Hagebusch, O. E.: Histaminase in the Treatment of Serum Sickness, J.A.M.A., 112:2398 (June 10), 1939.
- 37. Friedlaender, S. and Feinberg, S. M.: Histamine Antagonists. III.—The Effect of Oral and Local Use of Benadryl on the Whealing Due to Histamine, Antigen-Antibody Reactions, and Other Whealing Mechanisms. Therapeutic Results in Allergic Manifestations, J. Allergy, 17:129 (May), 1946.
- 38. Gaté, J., Thiers, H., Cuilleret, P., and Pellerat, J.: Recherches Sur l'Action de Nouveaux Composés Antihistaminiques de Synthése, J. de Méd., de Lyon, 23:401, 1942.
- 39. Ghiselin, A. D., Jr.: The Treatment of Seasonal and Non-Seasonal Hyperesthetic Rhinitis with Anthallan, Bull. New York Acad. Med., 22:320 (June), 1946.
- 40. Hansel, F. K.: Nethamine Hydrochloride and Theophylline Isobutanolamine in the Treatment of Nasal Allergy and Asthma, Ann. Allergy, 1:199 (Nov.-Dec.), 1943.
- 41. Hartman, M. M.: Parenteral Use of Butanefrine in Asthma. A Comparison with Epinephrine, Ann. Allergy, 3:366 (Sept.-Oct.), 1945.
- 42. Hartman, M. M.: Ethyl-nor-Epinephrine by Inhalation for Bronchial Asthma; A Comparison with Epinephrine, J. Allergy, 17:106 (March), 1946.
- 43. Hartman, M. M.: Fleabite Reactions—Clinical and Experimental Observations and Effect of Histamine-Azoprotein Therapy, Ann. Allergy, 4:131 (March-April), 1946.
- 44. Hartman, M. M.: Anti-Asthmatic Effects of Beta-Diethylaminoethyl 9, 10-Dihydroanthracene-9-Carboxylate Hydrochloride. A New Synthetic Antispasmodic, Ann. Allergy. To be published.
- 45. Horton, B. T.: The Use of Histamine in the Treatment of the Specific Types of Headaches, J.A.M.A., 116: 377 (Feb. 1), 1941.
- 46. Jacques, L. B. and Waters, E. T.: The Isolation of Crystalline Heparin from the Blood of Dogs in Anaphylactic Shock, Am. J. Physiol., 129:389, 1940.
- 47. Katz, G. and Cohen, S.: Experimental Evidence for Histamine Release in Allergy, J.A.M.A., 117:1782 (Nov. 22), 1941.
- 48. Koelsche, G. A., Prickman, L. E., and Carryer, H. M.: The Symptomatic Treatment of Bronchial Asthma and Hay Fever with Benadryl, Proc. Staff Meet., Mayo Clin., 20:432 1945.
  - 49. Landsteiner, K. and Lampl, H.: Über die Abhängig-

- keit der Serologischen Spezifizität von der Chemischen Struktur. XII.—Mitteilung Über Antigene, Biochem. Ztschr., 86:343, 1918.
- 50. Lehmann, G. and Knoefel, P. K.: The Spasmolytic and Local Anesthetic Action of Some Derivatives of Fluorene-Carboxylic Acid and Related Compounds, J. Pharmac. & Exper. Therap., 74:274 (March), 1942.
- 51. Levin, S. J.: Benadryl. Its Use in Allergic Diseases, J. Allergy, 17:145 (May), 1946.
- 52. Loew, E. R., Kaiser, M. E., and Moore, V.: Synthetic Benzhydryl Alkamine Ethers Effective in Preventing Fatal Experimental Asthma in Guinea Pigs Exposed to Atomized Histamine, J. Pharmacol. & Exper. Therap., 83:120,
- 53. Logan, G. B.: The Use of Benadryl in Treating Some of the Allergic Diseases of Childhood, Proc. Staff Meet., Mayo Clin., 20:436, 1945.
- 54. McElin, T. W. and Horton, B. T.: Clinical Observations on the Use of Benadryl, Proc. Sta- Meet., Mayo Clin., 20:417, 1945.
- 55. McGavack, T. H., Elias, H., and Boyd, L. J.: The Influence of Benadryl on Gastric Acidity, Gastroenterology, 6:439, 1946.
- 56. O'Leary, P. A. and Farber, E. M.: Benadryl in the Treatment of Urticaria, Proc. Staff Meet., Mayo Clin., 20:429, 1945.
- 57. Parrott, J. L.: Les Manifestations de l'Anaphylaxie et les Substances Histaminiques, Paris, 1938, Bailliére Edit.
- 58. Pinkus, H.: Benadryl in the Treatment of Erythema Exudativum Multiforme, Ann. Allergy, 4:288 (July-Aug.), 1946
- 59. Proetz, A. W.: Amino-Heptane As a Nasal Vasoconstrictor, Ann. Otol., Rhin. & Laryng., 51:112, 1942.
- Raymond, A. L.: Recent Developments in Synthetic Antispasmodics, J. Am. Pharmaceut. Assoc., Scientific Ed., 32:249 (Oct.), 1943.
- Rose, B.: Studies on Blood Histamine in Patients with Allergy. II.—Alterations in the Blood Histamine in Patients with Allergic Disease, J. Clin. Invest., 20:419, 1941
- 62. Scheinberg, D.: Generalized Angioneurotic Edema Due to Penicillin Inhalations Treated with Benadryl, J.A.M.A., 132:78 (Sept. 14), 1946.
- 63. Sheldon, J. M., Fell, N., Johnston, J. H., and Howes, H. A.: A Clinical Study of Histamine-Azoprotein in Allergic Disease, J. Allergy, 13:18, 1941.
- 64. Slater, B. J. and Francis, N.: Benadryl, A Contributing Cause of an Accident, J.A.M.A., 132:212 (Sept. 28), 1946.
- 65. State, D. and Wangensteen, O. W.: Procaine Intravenously in Treatment of Delayed Serum Sickness, J.A.M.A., 130:990 (April 13), 1946.
- 66. Thacker, E. A.: Evaluation of Benadryl as a Therapeutic Agent for Vasomotor and Allergic Rhinitis, Arch. Otorhinolaryng., 43:597 (June), 1946.
- 67. Todd, L. C.: Some Clinical Observations on the Use of Benadryl for the Symptomatic Relief of Allergic Conditions, Ann. Allergy, 4:282 (July-Aug.), 1946.
- 68. Waldbott, G. L.: Clinical Results with Benadryl, J. Allergy, 17:142 (May), 1946.
- 69. Wells, J. A., Morris, H. C., Bull, H. B., and Dragstedt, C. A.: Observations on the Nature of the Antagonism of Histamine by B-dimethylaminoethyl Benzhydryl Ether (Benadryl), J. Pharmacol. & Exper. Therap., 85:122,

#### MEDICAL PROGRESS:

# Progress in the Treatment Of Carcinoma of the Prostate

A. J. Scholl, M.D., Los Angeles

CARCINOMA of the prostate is a common and fatal disease although in many cases the life of the patient has been prolonged and made more livable by modern methods of treatment. The disease develops as a distinct pathologic entity and is apparently not related either to hyperplasia, inflammation or calculous involvement of the gland. In the majority of cases the tumor progresses slowly, metastasizes freely and usually causes death in a period measured by months. More rarely the growth may be sluggish, remaining confined to the prostate without noticable change for years, causing few if any symptoms, and the final confirming diagnosis in such cases may only be made at autopsy after death resulted from other causes.

#### INCIDENCE

Carcinoma occurs three times as frequently in the prostate as in any other internal organ of men. Young,30 in a review of his surgical cases, stated that carcinoma of the prostate is found in at least 14 per cent of all men over 44 years of age. About 20 per cent of men over 60 years will have prostatic trouble; four out of 20 of these will have carcinoma of the prostate. Rich26 reviewed 292 consecutive post mortem examinations of men aged 50 or over, who died of a wide variety of causes at the Johns Hopkins Hospital. Frank carcinoma of the prostate gland was observed in 31 cases in the microscopic section taken as a routine at autopsy. In 65.8 per cent of these 41 cases the tumor was not recognized clinically: in most instances it was too small to have produced symptoms or to have attracted attention on physical examination. Apparently the incidence of prostatic carcinoma increases with age. Moore 17 found prostatic cancer in 21 per cent of 252 subjects between 41 and 90 years of age; between the ages of 81 and 90 the incidence was 27 per cent. The same high incidence of occurrence is also reported from European medical centers. Walthard 29 examined 100 prostate glands of men more than 40 years of age. The specimens were obtained at necropsy. None of the patients had died from disease of the prostate gland. In 30 cases an undeniable carcinoma of the prostate was observed. In 25 cases signs of malignant infiltration had already occurred; in five cases the typical picture of carcinoma was observed without any infiltrating growth into the regional tissue. The reports of Rich and Walthard suggest that in a fair proportion of cases prostatic carcinoma may be entirely symptomless, causing no recognizable clinical disturbance to the host.

#### CLINICAL AND PATHOLOGIC DATA

The symptoms of carcinoma of the prostate are similar to those caused by prostatic hypertrophy. Both occur at approximately the same age and carcinoma is frequently super-imposed on benign hypertrophy. Rathbun<sup>24</sup> called attention to an important point in the history, namely, that the symptoms in cases of carcinoma are disproportionately severe in relation to their duration and the degree of obstruction present. Cachexia usually begins with marked urinary retention.

In a group of 280 cases reported by Barringer,2 carcinoma occurred most commonly between the ages of 65 and 69 years. In Young's cases the peak was 55 to 59. In a recent analysis of 581 cases by McCrea 16 the average age was found to be 63 years. The diagnosis of prostatic carcinoma, like the diagnosis of tumor of the bladder, is usually not made until the disease is far advanced. In Barringer's series of cases 24 months had elapsed between the onset of symptoms and the establishment of the diagnosis. In another group of 729 cases reviewed by McCrea the time of survival following admission to the hospital was nine months. Prostatic carcinoma rarely causes symptoms until the disease is far advanced, thus adding to the difficulty of its recognition in the early stages, which is the only time when a cure is possible. Persistent symptoms such as frequency and difficulty of urination, retention and nocturia among patients of carcinoma age should call for repeated careful examination for prostatic malignancy. If we expect to recognize this condition while it is still in a stage amenable to cure, periodic examinations of the prostate should be carried out in all men over 40 years of age, regardless of symptoms.

Clinically and pathologically there are two types of prostatic carcinoma, with, of course, intermediate stages. The first is the more common type. and its degree of malignancy is lower than that of the second type. The organ is made up of cells and glands and retains the normal or glandular structure. The cells are partly differentiated, fairly regular in size and shape, and retain the long tufted end projecting into the glandular lumen, which is the most significant feature of prostatic epithelium. The nuclei are round, relatively larger than the nuclei found in normal or hypertrophied glands. and contain the distinct nucleoli which are so prominent in undifferentiated cells. Clinically these prostates are large, nodular, stony, and produce the symptoms of obstruction first calling attention to

their presence.

The second type of cancer when examined microscopically may at times be confused with lymphocytic infiltration. The malignant cells that have migrated into the stroma often show a streaked or etched-out appearance, in contrast to the clumped, localized disposition of lymphocytic infiltration. The cells in such glands, either from morphologic or mechanical influences, have lost their original structure; they do not conform to the usual type, but vary in size and arrangement. These may comprise great masses or extending wedges of tightly packed cells containing large deeply staining nuclei. In other cases the cells may be loosely arranged, separated, and supported by a small amount of connective tissue. When there is an excessive amount of fibrous tissue, the cells may have disappeared completely or may be pressed into bizarre lines and streaks. If there is glandular formation the acini are atypical and the cells are flat, grouped together irregularly, and contain nuclei which are relatively much larger than those found in non-malignant cells. Clinically the prostates of this type are small, fibrous and firmly fixed. The tumors in them are extremely malignant, they metastasize readily, and they are often unrecognized, since paralysis may occur as a result of the metastasis before the gland has reached sufficient size to produce urinary symptoms. The small size of them often leads to the erroneous opinion that the patient is a good surgical risk and to operation with unfavorable results.

#### DIAGNOSIS

Rectal examination establishes the diagnosis in most cases. Unfortunately, in the large majority of cases the condition has advanced to such a stage that it is only too readily recognized. The prostate is firm, fixed with an unmistakable hardness, the lateral margins may be angular or the normal contour of the gland is completely obliterated. In a surprisingly large number of cases there is infiltration of the adjacent structures with an extension upward along the course of the seminal vesicles. In early cases only a hard nodule may be felt, or one side of the prostate is rigid with a fixed, sharp, lateral margin. In a small group of cases, either the growth itself is not particularly hard, or an overlying layer of adenomatous tissue masks the usual rigid firmness.

Cystoscopy usually reveals an unyielding area in the prostatic urethra that grips the instrument, causing a characteristic limitation of mobility. In a transurethral resection, malignant tissue cuts more cleanly and there is less bleeding than occurs with adenomatous hypertrophy, the edges of the cut tissue remain sharply defined and the tissue at times imparts a fibrous feeling to the instrument.

Determination of the acid phosphatase of the blood serum is a definite aid in diagnosis. It is known that there is a high concentration of acid phosphates in the prostate gland after puberty. Acid phosphatase is also present in the primary tumors of carcinomatous prostatic tissue, in the skeletel metastases and in the blood serum of the patients with metastases. The level of serum acid

phosphatase may be fairly high when extensive metastases are present. Nerb<sup>20</sup> states that comparable elevations in the blood are not found in any other condition and that the finding is pathognomonic. Only positive tests, that is, those indicating high levels, are of significance because, in some cases, there is no increase in the enzyme. If the growth is confined to the gland itself there is usually no increase in serum acid phosphatases; readings above 4 units are apparently diagnostic of metastases. Acid phosphatases readings may also be used as a determination of the efficacy of therapy. A decreasing level suggests clinical improvement; an increase signifies more extensive involvement and an unfavorable prognosis.

#### TREATMENT

The treatment of carcinoma of the prostate has always been unsatisfactory, the results poor. Only a small number of cases are seen early enough to be relieved by surgery, implanted radium gives at best questionable relief, only 5 per cent of tumors are sensitive to Roentgen rays (Barringer), and suprapubic drainage is an admission of failure. Truly this is a miserable outlook for the patient. In 1941 the discoveries of Huggins 12 offered these patients new hope—not necessarily hope of cure, but relief from suffering and the prolongation of a not uncomfortable life. Huggins and his co-workers demonstrated a functional relationship between prostatic carcinoma and certain endocrine substances, thus giving us an entirely new method of treatment.

The report of Bumpus<sup>4</sup> on 485 untreated patients with prostatic carcinoma is of interest and serves as a basis of comparison of the duration of life for them as against that for patients who have received treatment. In Bumpus' untreated cases the average duration of the disease until death was 31 months. When metastases had occurred at the time of examination, two-thirds of the patients died within nine months.

#### SURGERY

Radical removal. The only known cure for prostatic carcinoma is early radical removal of the gland. Both Young 30 and Hinman 11 have reported large series of cases with good survival rates and satisfactory functional results. A long period of survival should be expected in this group for, as pointed out by Hamm,9 these patients treated surgically represent cases selected in the early stages of the disease. This group also contains those patients in whom small areas of malignancy, undetected by the clinician or surgeon, were recognized and classified by the pathologist after removal. Colston<sup>5</sup> reported a series of 73 patients operated on at the Brady Institute during a five-year period; four died. Of 43 patients for whom the prognosis was good, 41 are living and well without evidence of metastasis or recurrence. Of 26 patients for whom the prognosis was poor, eight are living and well from three months to five years after operation. Follow-up of all patients who had early cancer on whom Young's radical operation was

performed showed that more than 50 per cent were free from trouble from five to twenty-seven years after leaving the hospital. Smith<sup>27</sup> reported 42 cases with three operative deaths. Seventeen died of the disease after an average duration of 27 months. Four are alive but have recurrence of their disease. Seventeen are alive and apparently well. Alcock<sup>1</sup> states that radical surgical removal offers the only possibility of curing the disease but that operation is applicable in such small percentage of cases that it is not an adequate solution of the problem. In 351 consecutive cases Barringer<sup>3</sup> found only 16 (4.5 per cent) which might be called reasonably small that were confined to the prostate gland and the periprostatic region. In a second group of 26 (7.4 per cent) cases, the growth was medium size, reaching well beyond the prostatic gland proper. In the remaining 309 (88 per cent) cases the growth was extensive and inoperable or there were metastases. Creevy6 advocates radical operation only in the earliest stages. In only ten of his 500 cases of prostatic carcinoma was the radical procedure done. In 95 per cent of Thompson's 28 cases the growth was spread beyond the confines of the prostate when first seen. Kahler<sup>15</sup> found an involvement of the perineural lymphatics in 91 per cent of cases of prostatic carcinoma. The localized tumors, even the smallest ones, showed this same high incidence of perineural involvement, an important argument against the feasibility of local removal in the majority of

There is a large group of patients with urinary obstruction but with such extensive growths that local removal is impossible. Until recently, suprapubic bladder drainage was employed in the majority of these patients. This made a very unhappy situation. The patient was constantly wet, the tube caused pain and required frequent attention, and in general this procedure made the last few months of life quite miserable.

Transurethral resection is the simplest and in the majority of cases the most satisfactory operation for the relief of obstructive urinary symptoms caused by prostatic carcinoma. If properly performed it gives adequate relief for prolonged intervals. Carcinomatous tissue resects easily and cleanly and the resection can be repeated if obstruction re-occurs. As Thompson states, normal vesical function is achieved at minimal risk to life, with practically no risk that incontinence will result.

#### ENDOCRINE THERAPY

A relationship between carcinoma of the prostate and certain hormones was demonstrated by Huggins in 1941. Since that time many patients with carcinoma of the prostate have been treated by castration and by the administration of estrogenic hormones. Dean, in discussing hormone therapy in these cases, states that, from the clinical viewpoint, the observations suggest that patients who have cancer of the prostate are made more comfortable when treated by surgical castration or by the administration of estrogens than when treated by other methods, and perhaps live longer.

The majority, however, after a variable period of improvement relapse and die of the disease. Possibly endocrine therapy exerts different degrees of benefit on different types of prostatic cancers to such a degree as to provide even a cure in an especially fortunate case.

Castration, thus decreasing the amount or the activity of the androgens, has been the most frequently employed method of changing the hormonal balance. Huggins 12 emphasizes that the results of castration in treatment of carcinoma of the prostate are not uniformly successful; they fall into three groups. In one group the patients (less than 5 per cent) receive no or slight benefit from this form of therapy. In the other groups, which were larger and contained nearly equal numbers of patients, improvement was pronounced but unsustained (less than 18 months) in the first, while in the second a pronounced and more prolonged regression of the disease was obtained.

There are a number of definite benefits which usually follow orchiectomy. Among the first of these is usually complete cessation of pain, with this relief in favorable cases persisting throughout the course of the disease. Patients who under earlier methods of treatment would require several grains of morphine daily are quite comfortable without sedation. Castration is also followed by a surprisingly pronounced feeling of well-being, together with a freedom from worry. Appetite improves and there is a gain in weight and strength. One patient with generalized bony metastases was able to resume his full duties as a Pullman porter shortly after orchiectomy; 18 months later he was still working. Pain was relieved in 88 per cent of Emmet's8 cases and favorable response as determined by both subjective and objective criteria was observed in 73 per cent of Nesbit's and Cumming's 21 cases. Huggins pointed out that frequently there is a recession of the primary tumor, so that the hard, nodular, craggy prostate gland becomes smooth and soft and greatly decreases in size. Changes are often observed in the metastatic growths in the bones on roentgenographic examination, the metastatic lesions usually undergoing increased calcification within several months after orchiectomy. The increased density is often followed by stabilization of growth or by disappearance of the metastatic growths to roentgenographic examination. The regressive changes in the prostate are at times quite marked. Regressive changes in the primary neoplasm occurred in 32 per cent of Emmet's cases and in a large portion of Nesbit's and Cumming's cases. Neuswanger<sup>24</sup> noticed two cases of incontinence following castration. The sphincter had weakened by invasion of carcinoma and castration caused so much relaxation that incontinence resulted.

There are a number of methods advocated for castration. The simplest and most effective is carried out by removing the testicle and epididymus through a small scrotal incision. The cord is clamped, cut and tied and the incision closed without drainage. A small amount of sulphanilimide placed in the wound prevents local infection and

acts as a hemostatic agent. Leaving part of the epididymis or the testicular shell for their prosthetic possibilities offers little and is rarely done at present. Munger<sup>19</sup> and others reported good results with destruction of the testicles by means of x-ray radiation.

#### ESTROGEN THERAPY

Estrogen therapy accomplishes much the same results as castration. Dean states that the clinical benefit which follows the oral administration of diethylstilbestrol is as great as that which follows surgical castration. Herbst 10 stated that the practical objective of chemical treatment of carcinoma is modification of the soil in which the malignant cells grow, in order to inhibit their growth. Huggins 14 states that the inhibition of the androgens is not complete in attempts at their inactivation by estrogens. Also the partial inhibition is temporary and estrogen therapy must be continued. Furthermore the administration of estrogen has in itself a carcinogenic effect.

There are a number of side effects which appear after the administration of estrogens, including nausea, reductions of sexual potency and mammary gland changes. The breasts frequently become swollen and painful, although in some cases no change is noted at any time. There is usually a microscopic proliferation as well as a gross enlargement of the breasts. Moore 18 and others have shown that the extent of the breast changes is no indication of the amount of benefit the patient is receiving. McCrea has noted that the side effects of estrogen therapy are less intense with ethinyl estradiol than with diethylstilbestrol.

A combination of castration and estrogen therapy is used in most cases; the results of the combined method will be discussed together. Castration should not be done routinely and there is no evidence that it is necessary in the early stages of the disease. Nesbit and Plumb<sup>22</sup> state that the preponderance of evidence continues to support the opinion that maximum therapeutic benefits are derived when the hormonal treatment of prostatic cancer is delayed until advanced stages of the disease have developed. It should be reserved for advanced cases and for those with metastases.

If the prostatic carcinoma is small, localized and can be removed surgically, radical resection should be considered. Some cases require no treatment. If the growth is inoperable, as is usually the case, and is causing neither pain nor urinary obstruction and is not increasing in size or metastasizing, watchful waiting is advisable. If treatment is indicated in the early stages of the disease, estrogens should be administered. If the patient does not respond to treatment or if the lesion is of the type which usually has a tendency to progress rapidly or if the patient cannot take stilbestrol, castration should be performed. Herbst showed that castration was effective for patients who showed no improvement after treatment with estrogens.

Castration should be reserved for the last play, for, once the testicles are removed, stilbestrol is of little value should there be a recurrence of symp-

toms. Also, castration involves the risk of provoking extra-gonadal production of androgens.

Nesbit and Plumb<sup>23</sup> reported a follow-up on 795 patients treated prior to the endocrine era and a comparison of survival rates between these and patients treated by endocrine therapy. Twelve months after first being seen, 7 per cent of those treated by stilbestrol and 18 per cent of those having had orchiectomy were dead, in contrast to a death rate of 48 per cent in those treated before 1940. At 24 months, 25 per cent of patients treated with stil-bestrol, 35 per cent of those having had orchiectomy and 68 per cent of the earlier group were dead. At 48 months, 65 per cent of those having had orchiectomy, and 80 per cent of the earlier treated cases were dead. Nesbit and Plumb reported that only 20 per cent of patients castrated for the treatment of prostatic cancer were living and free from symptoms after 41 months. Three-fourths of their patients who displayed no evidence of metastases when castrated were dead or, if alive, had widespread metastases.

#### SUMMARY

Carcinoma of the prostate is a frequently occurring fatal disease which usually causes symptoms only when far advanced. In order that this condition be recognized while still in a stage amenable to treatment, frequent periodic rectal examination must be done on all men over 40 years of age, regardless of symptoms.

If carcinoma is found in an operable stage, radical prostatectomy is usually indicated. When, as frequently occurs, the growth is inoperable and is causing symptoms, endocrine therapy is advisable either by the administration of estrogenic substances or castration or a combination of the two. Endocrine therapy relieves pain, retards the disease, prolongs life and in rare cases may be curative.

1930 Wilshire Boulevard, Los Angeles.

#### REFERENCES

- 1. Alcock, N. G.: In Discussion on Papers of Herbst, Moore and Others, Emmett and Greene, Bumpus and Others and Colston, J.A.M.A., 127:73 (Jan. 13), 1945.
- 2. Barringer, B. S.: Carcinoma of the Prostate, Ann. Surg., 93:326 (Jan.), 1931.
- 3. Barringer, B. S.: Prostatic Carcinoma, J. Urol., 33: 616 (June), 1935.
- 4. Bumpus, H. C., Jr.: Carcinoma of the Prostate, Surg. Gynec. Obst., 43:150-155 (Aug.), 1926.
- 5. Colston, J. A. C.: Surgical Removal of Cancer of the Prostate Gland: The Radical Operation, J.A.M.A., 127: 69-72 (Jan. 13), 1945.
- 6. Creevy, C. D.: In Discussion on Papers of Alyea and Henderson, Creevy, Thompson, Nesbit and Cummings, Gutman and Herbst, J.A.M.A., 120:1122 (Dec. 5), 1942.
- 7. Dean, A. L.: In Discussion on Papers of Alyea and Henderson and Chute, Willetts and Gens, J. Urol., 48:698-699 (Dec.), 1942.
- 8. Emmett, J. L., cited by Cummings, R. H., J.A.M.A., 127:72073 (Jan. 13), 1945.
- 9. Hamm, F. C.: Carcinoma of the Prostate: A Symposium, Clinical Aspects, Brooklyn Hospital Jour., IV:84-90 (Oct.), 1946.
- 10. Herbst, W. P.: The Effects of Biochemical Therapeusis in Carcinoma of the Prostate: Further Observations, J.A.M.A., 127:57-59 (Jan. 3), 1945.

- 11. Hinman, F. and Smith, D.: Carcinoma of the Prostate, Cal. & West. Med., 51:235-241 (Oct.), 1939.
- 12. Huggins, C., Stevens, R. E., and Hodges, C. V.: Studies (1. Prostatic Cancer: The Effect of Castration on Clinical Patients with Carcinoma of the Prostate, Arch. of Surg., 43:209, 1941.
- 13. Huggins, C.: Orchiectomy in the Treatment of Prostatic Cancer, J.A.M.A., 124:122 (Jan. 8), 1944.
- 14. Huggins, C.: A Summary of Endocrine Effects in Advanced Prostatic Cancer, New York State J. Med., 43: 519-521 (March 15), 1943.
- 15. Kahler, J. E.: Carcinoma of the Prostate Gland, Proc. Staff Meet., Mayo Clinic, 13:589-592 (Sept. 14), 1938.
- 16. McCrea, L. E.: Carcinoma of the Prostate: A Resume of Treatment with Ethinyl Estradiol, J. Urol., 56: 697-703 (Dec.), 1946.
- 17. Moore, R. A.: The Morphology of Small Prostatic Carcinoma, J. Urol., 33:224 (March), 1935.
- 18. Moore, G. F.: Wattenberg, C. A. and Rose, D. K.: Breast Changes Due to Diethylstilbestrol During Treatment of Cancer of the Prostate Gland, J.A.M.A., 127:60-62 (Jan. 13), 1945.
- 19. Munger, A. D.: In Discussion on Papers of Alyea and Henderson and Chute, Willets and Gens, J. Urol., 48:701-702 (Dec.), 1942.
- 20. Nerb, L.: Determination of the Acid Phosphates of the Blood Serum as an Aid in Diagnosis, Brooklyn Hospital Jour., 1V:91-93 (Oct.), 1946.
- 21. Nesbit, R. M. and Cummings, R. H.: Prostatic Car-

- cinoma Treated by Orchiectomy, J.A.M.A., 124:80-81 (Jan. 8), 1944.
- 22. Nesbit, R. M. and Plumb, R. T. (Unpublished Paper): Prostatic Carinoma Treated by Orchiectomy. Fourth Follow-up on a Series of 75 Cases, Forty-eight Months or More Postoperative.
- 23. Nesbit, R. M. and Plumb R. T.: Prostatic Carcinoma, Surgery, 20:263-272 (Aug.), 1946.
- 24. Neuswanger, C. H.: In Discussion on Papers of Alyea and Henderson and Chute, Willets and Gens, J. Urol., 48:694-697 (Dec.), 1942.
- 25. Rathbun, N. P.: Orchiectomy for Carcinoma of the Prostate: Personal Experiences, Trans. of the Am. Assn. of G. U. Surgery, 37:217-222, 1944.
- 26. Rich, A. R.: On the Frequency of Occurrence of Occult Carcinoma of the Prostate, J. Urol., 33:215 (March), 1935.
- 27. Smith, G. G.: Total Perineal Prostatectomy for Carcinoma, J. Urol., 35:610-617 (June), 1936.
- 28. Thompson, G. J.: Transurethral Resection of Malignant Lesions of the Prostate Gland, J.A.M.A., 120:1105-1109 (Dec. 5), 1942.
- 29. Walthard, B.: Die Haufigkeit und Histogenese des Prostatacarcinoms, Ztschr. f. Urol. Chir. u. Gynak., 43: 483-496 (Jan.), 1938.
- 30. Young, H. H.: The Cure of Cancer of the Prostate by Radical Perineal Prostectomy (Prostato-Seminal Vesiculectomy): History, Literature and Statistics of Young's Operation, J. Urol., 53:188-256 (Jan.), 1945.

Cy

76th Annual Session

California Medical Association

Los Angeles

April 30—May 3, 1947

# Palifornia MEDICINE

OWNED AND PUBLISHED BY THE CALIFORNIA MEDICAL ASSOCIATION
450 SUTTER, SAN FRANCISCO 8 , PHONE DOUGLAS 0062

EDITOR, DWIGHT L. WILBUR, M.D. ASSISTANT TO THE EDITOR, ROBERT F. EDWARDS EDITORIAL EXECUTIVE COMMITTEE

LAMBERT B. COBLENTZ, San Francisco

ALBERT J. SCHOLL, Los Angeles

H. J. TEMPLETON, Oakland

For Information on Preparation of Manuscript, See Advertising Page 2

## EDITORIALS

### The Relation of the General Practitioner to the Practice of Medicine in Hospitals

The place of the General Practitioner in the practice of medicine in the hospital is a subject that lately has been discussed heatedly and widely by the medical profession. This problem can be answered only after answering two other questions. First, what is the place of the General Practitioner in the practice of medicine? Second, what is the place of the hospital in the practice of medicine?

The training of a doctor of today is inextricably combined with hospital facilities. The use of hospital facilities is now recognized by most people as the sine qua non of adequate medical care. It has been estimated that about 80 per cent of the practice of medicine is taken care of by the General Practitioner and about 20 per cent by the Specialist. It seems to follow that if hospital facilities are inseparable from the present day concept of adequate medical care and if 80 per cent of the medical care of the nation is in the hands of the General Practitioners who have been trained to use the hospitals, then to eliminate or exclude the General Practitioner from the use of hospital facilities perpetrates a fraud on the public and on the doctor who has been trained to use those facilities. Such exclusion would inevitably result in lower standards of care for the bulk of his patients.

The use of hospitals as a place for the practice of Specialists alone is a relatively recent development. The tendency began in a laudable effort instituted by the American Medical Association and later brought to fruition by the admirable work of the American College of Surgeons to raise hospital standards. From a totally unorganized, unstandardized jumble of good and bad hospital facilities has come our present-day American hospital system. The purpose of the American Medical Association and the American College of Surgeons

has been not to eliminate capable doctors from staffs nor to concentrate the practice of medicine in the hands of the few. The fact that such a development seems to be arising is rather the fault of administration and a failure to analyze and direct the hospital system.

The purpose of the Certification Boards of Specialists has been stated admirably by the American Board of Surgery in a resolution passed by that Board December 14, 1946. Among other things this resolution stated: "The American Board of Surgery is not concerned with measures that might gain special privileges of recognition for its certificants in the practice of surgery. It is neither the intent nor has it been the purpose of the Board to define requirements for membership on the staffs of hospitals. The Board specifically disclaims interest in or recognition of differential emoluments that may be based on certification."

This is a clear statement and is unassailable. However, in the book "The American Hospital"—1946 edition, page 155, the author, Dr. Corwin (Ph.D.), states: "In the future there will be no excuse to make a major hospital staff appointment from among any except those who have met the standards of their respective Specialty Boards."

Many hospitals have turned lately toward Dr. Corwin's concept of staff appointments so that at present it is practically hopeless for a General Practitioner to apply for membership on a major hospital staff, at least in the larger cities. These hospitals explain this attitude by the statement that they have not enough beds to supply the demands of the men already on the staffs (and this is absolutely true). Also, they have stated that they could not allow any except Specialists or Diplomates of the Specialty Boards as members of the staff or

heads of department, else they would lose their approval as training hospitals for Residents. By unanimous vote the House of Delegates of the American Medical Association, on December 10, 1946, at the Chicago meeting, settled this aspect of the question by adopting the resolution reading as follows:

"Resolved, that hospitals should be encouraged to establish General Practitioner services. Appointments to a General Practice Section shall be made by the hospital authorities on the merits and training of the physician. Such a General Practice Section shall not per se prevent approval of a hospital for the training of Internes and Residencies. The criterion of whether a physician may be member of a hospital staff should not be dependent on certification by the various Specialty Boards or membership in special societies."

Despite the specific disclaimer by the American Board of Surgery of its interest in any recognition of differential emoluments based on certification, various hospitals and notably government bureaus (for instance, the Veterans' Administration) have added 25 per cent more pay or differential in fees to those who are certified. This definitely is opposed to the objects of the Board and inevitably causes unrest and apprehension among other capable men who see in this action (rightly or wrongly) a plan to concentrate all hospital practice in the hands of a few.

It is apparent from these facts that the principles stated by the various corollary organizations of medicine are not at fault. In the development of staffs of hospitals limited to specialists, therefore, there has been misinterpretation or maladministration of these principles.

We are now in battle again in our legislature, fighting enactment of bills under the guise of hospitalization insurance, which would destroy the proper practice of medicine and would perpetrate a fraud on the public. The greatest weapon against the enactment of these Compulsory Health Insurance schemes has been the development by medicine of voluntary pre-payment plans to finance the cost of medical care and hospitalization. These plans have been supported by the general practitioners of medicine. Those few doctors who have obstructed, or at most given luke warm participation to those plans, have been in the main specialists. Under the contracts of the voluntary plans, such as California Physicians' Service, and others, practically all the conditions covered by the policies consist of surgical or other procedures listed under specialty classification. If a General Practitioner is not admitted to hospital practice to care for those procedures simply because he is not a Specialist, rather than upon a basis of his ability to perform that type of service, it follows that he cannot long support these voluntary medical service plans. For him not to support these plans would be disastrous, as it would then be relatively simple for a disappointed public to succumb to the false promises and blandishments of politically ambitious schemers who promise Utopia under the guise of socialized medicine. As stated before, the government bureaus

have already given evidence that they would draw the lines of specialism tighter and would strangle the very thing we are trying to preserve for the people.

It was evidently many of these considerations that prompted the House of Delegates of the American Medical Association to pass the resolution urging establishment of General Practitioner Sections in all hospitals, and to point out that the ability of a doctor is the governing factor for good service rather than membership in any special society.

It is imperative of course to restrict, by proper consultation and rules, the performance of any medical or surgical procedure to those who have proved their capability. This is well recognized and accepted by all. The proof of the pudding is in the eating. Actual performance, or as Al Smith said, "a look at the record" could easily enable a doctor to be judged on his merits. The need for specialism is self evident. The worth of the Specialist and his use of hospital facilities for the benefit of his patients needs no apologia.

In addition it would seem that the General Practitioner is well within his rights to ask—and the welfare of his patients (constituting 80 per cent of all the people needing medical care) demands—that hospitals heed at once the dictum of the House of Delegates of the American Medical Association and take steps to rectify a trend or a policy of action that is so fraught with danger, injustice and lack of wisdom.

### **Nursing at the Crossroads**

The current session of the State Legislature highlights the situation faced by California and the nation in the matter of adequate nursing facilities. There are before the members of the Legislature several bills aimed at ameliorating the shortage which is little short of startling.

On the one hand there is a bill to abolish a present section of the Medical Practice Act which provides for the licensing of "trained attendants" for hospital service. At the other extreme is a bill which would build this section up into a provision for a completely new licensing board, the majority of the members of which would be members of the State Board of Nurse Examiners. This latter measure would standardize on a nine months training course for trained attendants and would presumably create a corps of hospital attendants who could properly handle numerous duties in the care of patients under the supervision of registered nurses, the latter then to act as administrators of wards or other hospital units. The present law on trained attendants dates back to 1935. In the first year after its passage there were nine persons licensed under its terms by the Board of Medical Examiners; in the succeeding ten years there have been exactly two persons licensed.

Everyone associated with the care of the sick knows of the serious shortage of nurses; those closest to the picture know that many nurse training schools have been unable to fill their student classes this year. The cause of this shortage may be the availability of other work at more attractive wages, or it may be the desire to get away from some of the more unpleasant tasks of nursing. Whatever the reason, the fact remains that nurses are scarce and that many of them, fully trained, are seeking other occupations or are at least remaining out of active practice.

Nurse organizations have been reluctant to condone the services of practical nurses for home duty, or nurses' aides (or other attendants) for hospital duty. Previous proposals for legislation along these lines have met with opposition from the higher echelons of the nursing profession. However, we have all witnessed the invaluable work of Red Cross nurses' aides during the war years and many have seen the satisfactory work of hospital corpsmen in the Army and Navy under the trying conditions of service. Some of these corpsmen were trained for as little as three months. Others were given more extensive schooling. The shorter period was to qualify the corpsman for ward duty, and the longer courses for surgical, laboratory or other specialized services. Their great value in wartime argues for the use of

similar attendants in peace. In the words of one California physician, "You don't need a Ph. D. to carry a bedpan."

That the shortage of nursing care is not peculiar to California is demonstrated in the activities of the American College of Surgeons and the American Surgical Association, which have launched nationwide inquiries into nursing and which have hope of arriving at solutions which can be applied here and elsewhere. It can be expected that some system of nurse supervisors and less fully trained attendants will probably emerge from their studies.

The members of the California Medical Association are vitally interested in this problem. They are faced with the diametrically opposed bills now before the Legislature in Sacramento. The decision of their Legislative Committee at this writing is that the proposals in Sacramento should be deferred until a complete re-evaluation of the entire nursing situation can be brought out by the national bodies studying the problem. Then we can hope for a progressive program which will place the proper emphasis on all angles of a complex problem and result in a solution in the public interest.



76th Annual Session
California Medical Association
Los Angeles
April 30—May 3, 1947

#### CLINICAL CONFERENCE

## Acute Transient Pancreatitis Associated with Chronic Cholecystitis and Cholelithiasis

From the University of California Surgical Service of the San Francisco Hospital, February 25, 1947

Presentation of the Case by the House Officer, Dr. Louis Nash:

A 58-year-old white woman entered the hospital January 20, 1947, complaining of abdominal pain of two days' duration. Two days before entry, shortly after lunch, she experienced severe epigastric pain which had a sudden onset, was steady, and remained constant. The pain was sharp and piercing and radiated to the left lower quadrant, but not to the back or shoulder. There was persistent anorexia and nausea and vomiting occurred several times. The vomitus was green in color and did not contain blood. Stools and urine were normal; there were no chills or fever. The patient was completely prostrated and remained in bed from the onset of the episode until entry into the hospital.

Twelve years before, she had had colicky upper abdominal pain, followed by jaundice, which lasted two weeks. At that time the urine was dark and stools were light in color. An episode of pain and nausea similar to the present attack occurred two months before entry, but subsided abruptly after about two hours. The past history was not remarkable otherwise. There were five children. Menses had not occurred for the past ten years, but interview elicited no other menopausal symptoms. Use of alcohol or tobacco was denied.

On entry, the temperature was 38.5°C.; pulse was 92 and respiration 16 per minute; blood pressure was 130/70. Examination showed a moderately obese, cooperative woman appearing about the stated age of 58 years. The abdomen was rounded and showed no scars. There was moderate tenderness to palpation over the entire upper abdomen, most marked in the epigastrium. There was no muscle spasm, but some voluntary guarding. Questionable rebound tenderness was elicited in the epigastrium. No organs or masses were palpable. Peristalsis was hypoactive. Pelvic and rectal examination revealed no tenderness in these areas.

Urinalysis showed no sugar or albumin; urobilinogen was positive 1:1, negative 1:10; microscopic examination showed 20 white blood cells

per high dry field. Hemoglobin was 13.4 gm. and white blood count was 21,000 with 84 per cent neutrophiles, 15 per cent lymphocytes and 1 per cent monocytes. The corrected sedimentation rate was 4 mm. in one hour. Serum amylase was 890 units. Total serum protein was 8.4 gm. per cent; albumin, 4.1 gm. per cent; globulin, 4.3 gm. per cent. Icteric index was 11 units. Wassermann reaction was negative. An x-ray film of the abdomen showed no evidence of disease. The gallbladder was not made visible by intravenous cholecystography.

Supportive treatment with intravenous fluids was given. Temperature became normal on the fifth hospital day and abdominal pain and nausea gradually subsided. On the ninth hospital day intravenous cholecystograms were repeated and still showed a non-functioning gallbladder. Additional laboratory studies during the hospital stay are shown in Table 1. The patient was discharged January 30, 1947.

On February 15, 1947, the patient was readmitted to the hospital for cholecystectomy. While at home there was no pain and the patient had been able to eat anything without distress. Examination on admission showed no abdominal tenderness. Temperature was 37.2°C. Serum amylase was 23 units; blood cholesterol, 212 mg. per cent; prothrombin, 90 per cent of normal; hippuric acid, 1.4 gm. White blood cell count was 9,600 with 62

per cent polymorphonuclear cells.

On February 19, 1947, cholecystectomy and exploration of the common bile duct were carried out. No free fluid was present in the peritoneum. Small, pale, 3 mm.-sized areas of old fat necrosis were grossly visible over the mesentery, omentum, and hepatic surface. The gallbladder was of normal size, not acutely inflammed, and contained many small cholesterol calcium bilirubinate stones. The cystic duct was 7 to 8 mm. in diameter and large enough for the smaller stones to pass. The common duct was about twice normal size but thin walled and free from stones or any type of obstruction. The pancreas was twice normal size and very diffusely firm and lobular, particularly about the

TABLE 1.—Serial Laboratory and Clinical Studies

Hospital Day							
1	2	3	4	5	6	7	8
Serum amylase (units). 890	298	290	148	40		253	
Urine amylase (units)	413	1,057	338	595		795	19
Temperature38.9°C.	38.4	38.3	37.8	37.3	37.2		
Abdominal pain $\dots + + +$	+	+ .	none	none	none		
White blood cells21,000	13,900					11,500	
Icteric index (units) 11		5					

The gallbladder was removed and the common duct drained with a "T" tube. Analysis showed the gallbladder bile amylase to be 925 units, and the common duct bile amylase 85 units.

The patient's postoperative course was uncomplicated. Temperature, which was 38.3°C. on the first day, became normal on the second day. Bile drainage was 300 to 350 cc. per day.

#### CLINICAL DISCUSSION

DR. CLAYTON G. LYON\*: The elevated serum amylase levels, and the amylase in the urine and gallbladder bile show that this is a case of acute pancreatitis. Everyone may recall cases which were called alcoholic hepatitis or gastritis, which proved to be acute pancreatitic edema or acute hemorrhagic pancreatitis. It has been found that alcoholism is associated with acute pancreatic disease more frequently than with gallbladder disease. Direct trauma may also cause acute pancreatitis.

DR. ALBERT G. CLARK†: In making a diagnosis on the basis of serum amylase levels, I think it should be emphasized that in a private hospital, where these tests are not done often, the findings are not reliable. Here one is fairly sure of the laboratory work.

DR. RALPH CRESSMAN††: If the patient is acutely ill, immediate removal of blood for the serum amylase may be followed by intravenous administration of the gallbladder dye; in the morning the x-ray may be taken. We have seen patients with acute pancreatitis in whom the first cholecvstographic films did not show a visualizing gallbladder but in whom the second films did.

Dr. STANLEY G. JOHNSON\*\*: Speculation as to the etiologic factors is interesting. The following pathogenic factors may contribute at some time or other: (1) Bile reflux into pancreatic duct secondary to partial or complete occlusion of ampulla by a stone, (2) Spasm of the ampullary sphincter, (3) Obstruction of the pancreatic duct by stone or spasm, (4) Extension of inflammatory process to the pancreas by anatomical continuity, (5) Erosion of ulcer of stomach or duodenum into the pancreas, (6) Trauma to the pancreas, (7) Excessive alcoholism, (8) Infarction of pancreas. The disease can mimic any acute intra-abdominal process, though at times its manifestations are quite typical, as they were in this patient. It is a common disease that is rarely fatal.

In all cases, but particularly in the atypical case, the serum amylase test supplies our most dependable single datum. There occurs a sharp rise in serum amylase with the onset of the disease which, in the majority of cases, declines sharply to a normal level in 24 to 72 hours. The implications are obvious. When the patient enters the hospital

24 to 48 hours after the onset of symptoms, or even later, elevated urinary amylase readings present at that time can help us to arrive at the diagnosis.

Acute infection of the salivary glands or obstruction of their ducts, and impaired renal function with subsequent retention of amylase, will also result in elevated levels. The former condition should be obvious, and a comparison of serum and urinary amylase levels should indicate the latter, in which the serum level usually is only high enough to make the situation equivocal.

Dr. Leon Goldmant: This patient demonstrates a number of factors. In the literature the percentage of patients with acute pancreatitis who were believed to have associated gallbladder disease is quoted as being 60 per cent. In this hospital, because of the higher incidence of alcoholism in our patients, the percentage of cholecystic disease is much lower. This patient had a history of gallbladder disease and at one time was said to have had symptoms suggestive of a common duct stone with obstructive jaundice. At the onset of the pancreatitis there was persistent vomiting, which is a common symptom in most of these patients. The pain was not over the gallbladder region, and the rigidity was too mild to suggest a perforated peptic ulcer. There was no back pain or glycosuria. A normal blood amylase does not rule out acute pancreatitis, as the amylase level may return to normal a few hours after the onset of the attack of pain. The height of the serum amylase level does not differentiate acute pancreatic necrosis from acute transient pancreatitis, as it is probable that they are both different manifestations of the same pathological process. The urinary amylase is a valuable test when the patient is seen after the early symptoms have subsided, since its elevation lags behind that of the serum amylase. Another interesting finding in this patient is amylase of 925 units in the gallbladder bile, which probably results from a reflux of pancreatic enzymes into the gallbladder.

If the presence of gallstones in this patient is the etiological factor in the production of pancreatitis, then removal of the gallbladder and exploration of the common duct should be of some aid in avoiding a recurrence. Subsequent stricture around the lower end of the common duct due to stenosing fibrous chronic pancreatitis is a rare sequela. Therefore, it is important that the "T" tube which drains the common duct be left in place for three or four months. Cholangiograms should be taken before it is removed. If the tube is removed before the process is completely healed, chronic fibrosing obstruction of the bile duct may develop later. The mechanism in this patient might be due to the reflux of bile, lodgment of a small stone in the ampulla, or spasm of the ampullary sphincter. We know that the serum amylase elevation occurs in acute pancreatitis but not in chronic pancreatitis. These amylase tests actually are simple to do: they are not much more difficult than blood

<sup>\*</sup> Assistant Clinical Professor of Surgery, University of California School of Medicine, San Francisco.

<sup>†</sup> Clinical Instructor in Surgery, University of California School of Medicine, San Francisco.

<sup>††</sup> Clinical Instructor in Surgery, University of California School of Medicine, San Francisco.

<sup>\*\*</sup> Clinical Instructor in Surgery, University of California School of Medicine, San Francisco.

<sup>‡</sup> Associate Professor of Surgery, University of California School of Medicine, San Francisco.

sugar tests and should be available in any hospital where patients with acute abdominal conditions are admitted.

The differentiation of acute pancreatitis into the hemorrhagic or transient type is made clinically. In the hemorrhagic type, which is often associated with shock, the mortality rate is approximately 50 per cent, whether or not operation is carried out. If one should operate upon such a patient, one drains the gallbladder and lesser peritoneal sac.

Many of these patients develop abscesses of the lesser peritoneal sac, which occur late and are more

an accumulation of necrotic material than a collection of pus. These abscesses usually do not resolve spontaneously, but must be drained. Rarely cysts or pseudocysts of the pancreas form after pancreatitis. It is possible for a patient to have acute pancreatitis associated with acute gallbladder colic, and possibly stones, and to have a recurrence of pain even after gallbladder removal. The pancreatitis may cause the symptoms ascribed to gallbladder disease. The reason for removing the gallbladder is the possibility of the patient's forming other stones in the gallbladder.

#### 80 VOLUNTARY HEALTH PLANS IN 33 STATES COVER FOUR MILLION

"Driving to complete the voluntary health insurance program for the care of the American people is the big job facing local, state and national medical organizations today," according to Thomas A. Hendricks, secretary of the Council on Medical Service of the American Medical Association. "More than 80 plans sponsored by medical societies in 33 states covering 4,000,000 persons are now in operation and the task has just begun.

"The pioneering state of voluntary health insurance is nearing completion and, nationally, we are rapidly entering the development stage. Only two states do not have a plan operating or in the process of formation. Plans for a prepayment program are now being made in 13 states and the District of Columbia. Growth of the plans now in operation has been rapid, the over-all expansion within the last six months being as phenomenal a production figure as has appeared in modern insurance records.

"The enrollment in prepayment plans has accelerated slowly. This was partly due to the difficulties developed in the early experimental stages through which such plans had to pass, and partly to hesitancy on the part of doctors to plunge into an untested field of endeavor. As the number of plans has increased, so too has the acceleration in enrollment. During 1945 the over-all increase was 114 per cent. For the first six months of 1946 the enrollment increase was approximately 40 per cent, bringing the total to nearly the 4,000.000 mark. Indications are that enrollment will reach 5,000,000 by early 1947.

"One of the objectives of the Council on Medical Service is to present the facts in regard to advantages and disadvantages of the various plans, keep records up to date on all new developments in the medical care field, conciliate differences of opinion as to the various forms of insurance—in short, view the entire question impartially and objectively, in order to do everything possible to encourage the wholehearted acceptance by every state society of a practical, workable plan.

"The whole insurance program is still experimental. No one knows the complete answer. Hence, the council hopes to encourage all types of plans that meet the minimum requirements set by the council to maintain the standard of medical service for the protection of the public.

"The council is now set up to do the job of (1) encouraging development of new plans; (2) keeping the

profession informed as to developments, and (3) helping to increase the enrollment of plans already established.

"A prepayment division of the council has been created with George Cooley, assistant secretary of the council, keeping in contact with medical society-sponsored plans; Howard Brower, maintaining contact with private insurance groups; and L. S. Kleinschmidt, concentrating his efforts on encouraging rural enrollment and maintaining contact with the newly created consumer-operative movement.

"Prepayment plans have progressed rapidly in the cities, but development in the rural areas has been slow, although several plans have been making notable advancements along this line.

"Jay Ketchum, Lansing, executive vice president of Michigan Medical Service, is acting as consultant for the council.

"Within the past few months private insurance carriers are showing an intense interest in medical and surgical care coverage and, as a result, there have been many conferences both formal and informal. A joint conference was held with representatives of large insurance associations in Chicago in September, with Dr. E. J. McCormick, of Toledo, chairman of the council, presiding.

"One of the most important developments has been the creation of Associated Medical Care Plans, with Dr. H. L. Schriver, of Cincinnati, Ohio, as president; William M. Bowman, San Francisco, vice president; Jay Ketchum, secretary; and Dr. Norman Scott, Newark, N. J., treasurer. In a sense this is a trade organization of plans. It can be of great service in developing reciprocity, details of selling, cooperative actions and procedure. Frank Smith, who has served with the California Physicians' Service, San Francisco, as director of public relations, recently has been appointed A.M.C.P. director. Although A.M.C.P. will be housed with the council and its work integrated with the work of the council and in accord with the policies of the council, it is a legal entity separate and distinct from the council. The board of trustees has allotted through the council sufficient funds to this organization to get started.

"The council is also aided by Frank Dickinson, Ph.D., director of the Bureau of Medical Economic Research of the American Medical Association, and T. V. McDavitt of the A.M.A. staff has served as the legal advisor of A.M.C.P."



## CALIFORNIA MEDICAL ASSOCIATION

FOR COMPLETE ROSTER OF OFFICERS, SEE ADVERTISING PAGE 4

### **NOTICES AND REPORTS**

## NEWS of the DAY in the C.M.A.

March 2—Joint legislative meeting today with dentists, pharmacists, dispensing opticians, hospitals, etc. This program now five years old and its worth proved in elimination of inter-professional differences. Bill proposed by each group looked over by all, amendments offered and accepted. Now when we get to Sacramento there is unified opinion among allied groups rather than differences. Two or three of these sessions each legislative year.

March 4—Checking up today on eastern sanitarium where patient of California physician has ended up under poultice treatment for cancer. Looks as though patient would be better off to return to her own doctor here.

March 5-6—Catching up with first-of-month business, correspondence, billing, etc. Funny how the mail can accumulate without notice, each item posing another problem and each demanding attention right now. Somehow the stack never seems to get any lower but somehow it manages to get done without too big a backlog piling up.

March 7—Final touches put on Executive Committee meeting agenda and transportation picked up for San Francisco-Los Angeles. What with busy programs for everybody, arranging meetings is not so easy as it used to be. All sigh with relief when a quorum is assured.

March 8—Executive Committee meets in Los Angeles, discusses mutual problems with president of New Mexico Physicians' Service, a prepayment plan patterned after C.P.S and actively sponsored by C.M.A. Plan has been operating for eight months and shows visible signs of progress. Management appears splendid and prospects good. Executive Committee to report findings to Council next week. C.P.S. Executive Committee also meets in Los Angeles today, preparatory to Trustees' meeting Sunday.

March 9-C.P.S. Trustees meet, cover full-day agenda and vote to hold regular metings third

Sunday of each month from now on. Business has grown to size where meetings every eight weeks, more recently every six, no longer suffice to meet demands. Comparison of monthly business for past five years shows growth from \$70,000 monthly revenue to \$620,000. Add that to service rendered for Veterans' Administration and annual business runs to better than \$12,000,000. Which is no peanuts, nor hay.

March 10-11—Finishing touches put on printing of Annual Session program. Pre-convention number of Journal to be March issue this year and all set for it. Programs are all timed, speakers limited to set periods, and interval-timers readied for chairmen. Now you can go to hear one paper in one section and count on being on time to hear another in another meeting. Committee on Scientific Work has worked out all details down to final minute and it looks good on paper.

March 9—Income tax day. 'Nuff said. Advisory Planning Committee meets in morning, Council at lunch and all afternoon, recesses until Sunday. Council meetings now planned as day-and-a-half affairs to cover business presented.

March 16—Council reconvenes and sits from 9:30 a.m. to 5:50 p.m. Thirty men for eight hours plus, on top of five hours plus on Saturday—that's a lot of man-hours. The C.I.O. would demand double for overtime on that schedule.

March 17 — Legislature reconvenes in Sacramento, putting on two-ring show of regular and special sessions running concurrently. If the highway problems of the special session can be resolved, the 4,100 bills introduced in the regular session can be put on the calendar. Fortunately, only 450 of these affect the public health or the practice of medicine but that takes a lot of watching. For the next few months we can figure on a lot of time spent on legislative activities.

March 18—More conference on New Mexico situation and on general business. Visit from

another delegate on way to Honolulu to look into proposal for compulsory health insurance there. Seems to be catching.

March 19—Council minutes prepared, and a long set of minutes they are, complete with 33 pages taken by court reporter on stenotype machine. Most of the day spent on typewriter on minutes and on other writing which needs doing and takes time which seems lacking.

March 20—California delegation off to Salt Lake City today for annual meeting of United Public Health League. Delegates from ten states expected and report due from Washington, D. C., representative. Program is to set up office on train and work out details enroute. Good system, too.

March 22—United Public Health League meets in Hotel Utah, which is crowded to capacity by high school students from all over Utah, here for annual high school basketball tournament. More bobby sox seen in hotel lobby than at any time

since Sinatra's last appearance. Meeting big success; state representatives enthusiastic over League program.

March 24—Back to Sacramento and San Francisco. Committee hearings getting under way on various bills. From now on it's keep your eyes open and your powder dry. Many bills lead feline lives and it's hard to tell when they're dead. By the same token, you can't count on a bill having passed until it's voted, printed, engrossed and signed.

March 27-28—The Cancer Commission of the C.M.A. conducted a very successful refresher course on Neoplastic Diseases at Stanford and University of California Medical Schools. Regrettable that all of the applicants could not be registered in this excellent and informative session. This is not the last of the courses, and hope is that, in the future larger meeting rooms may be secured.

### **Council Meeting Minutes**

Tentative Draft, Minutes of the 339th Meeting of the Council, California Medical Association San Francisco, March 15-16, 1947

The meeting was called to order by Chairman Edwin L. Bruck at 1:30 p.m., Saturday, March 15, 1947, at the Fairmont Hotel, San Francisco.

#### 1. Roll Call:

Present were President McClendon, President-Elect Cline, Speaker Askey, Vice-Speaker Alesen, Secretary Garland, Editor Wilbur and Councilors Bruck, Shipman, Crane, Henderson, Anderson, Kneeshaw, Kindall, MacDonald, Green, Cherry, MacLean, Moody, Thompson and Regan.

Absent: Councilor Johnston. A quorum present and acting.

Present by invitation were Doctor C. L. Cooley, secretary of California Physicians' Service; Doctor D. H. Murray, chairman of the Committee on Public Policy and Legislation; Mr. Clem Whitaker, public relations consultant; Mr. W. M. Bowman, executive director of C.P.S.; executive secretaries Kihm of San Francisco, Young of San Diego, Waterson of Alameda and Donovan of Santa Clara County; Mr. Howard Hassard and Mr. Hartley F. Peart, legal counsel; Mr. John Hunton, executive secretary and Mr. William P. Wheeler, assistant executive secretary.

#### 2. Approval of Minutes:

- (a) Minutes of the 338th Council Meeting held January 12, 1947, were approved.
- (b) Minutes of the 200th Meeting of Executive Committee, January 22, 1947, were approved.
- (c) Minutes of the 201st Meeting of Executive Committee, February 5, 1947, were approved.
- (d) Minutes of the 202nd Meeting of Executive Committee, March 8, 1947, were approved.

#### 3. Membership: Wolff and Bayer Appeals.

At this point, the Council went into executive session, with Messrs. Hassard and Hunton present, to hear an appeal by Doctors Ernst Wolff and Leona Bayer of San Francisco on the ruling by the San Francisco County Medical Society that their memberships had lapsed by reason of non-payment of dues before the final date set for such payment. A stenotype reporter was present and recorded the entire proceeding.

- (a) A report of membership as of March 14, 1947, was received.
- (b) On motion duly made and seconded, it was voted to reinstate to active membership 14 members whose 1946 dues had been received since January 12, 1947.
- (c) On motion duly made and seconded, it was voted to grant Retired Membership to 38 members who had been nominated by their respective county societies.
- (d) On motion duly made and seconded, it was voted to grant Associate Membership to six members nominated by their respective county societies
- (e) On motion duly made and seconded, Doctor G. David Kelker of San Luis Obispo County was elected to Life Membership under the terms of provision (1) of Article IV, Section 1(e) of the Constitution. In this connection, it was moved by Shipman, seconded by Henderson and unanimously voted that legal counsel be instructed to reword Article IV, Section 1(e) of the Constitution in order to eliminate possible ambiguity. Such rewording would be presented by the Council as a

proposed Constitutional amendment to the House of Delegates.

- (f) A request by the San Francisco County Medical Society to grant retired membership to two members whose applications did not conform to Constitutional requirements was tabled.
- (g) A request by the Sacramento Society for Medical Improvement for possible relief from dues for three returned veteran members now engaged in postgraduate study was discussed. The Secretary was instructed to reply to the effect that such relief was not within the jurisdiction of the Council and to suggest that such members either be granted Associate membership or drop out of membership during the terms of their postgraduate studies.

#### 4. 1947 Annual Session:

- (a) Doctor H. V. Allington of Alameda County appeared before the Council with a request from the Section on Dermatology that one of the 1947 Annual Session guest speakers be selected from a proposed list of dermatologists as recognition of the 25th anniversary of the formation of this section. The Chairman of the Committee on Scientific Work referred to correspondence over a period of several months on this subject, and it was pointed out that the 1947 program had already been completed and set in type preparatory to printing. On motion duly made and seconded, it was unanimously voted that the Chairman of the Committee on Scientific Work apprise the representatives of the Section on Dermatology of the condition which now exists with regard to the program for the 1947 Annual Session and call attention to the correspondence which has already taken place on this request.
- (b) Doctor Kindall outlined some proposed entertainment for the President's Dinner at the Annual Session. It was moved by Alesen, seconded by Thompson and voted that Doctor Kindall be authorized to continue with such plans at a cost not to exceed \$350.
- (c) On motion duly made and seconded, it was voted to meet the request of the Woman's Auxiliary for an appropriation of \$750 to help defray the expenses of the annual meeting of the Auxiliary.
- (d) Doctor Askey brought up a question which had been raised in regard to a proposed Constitutional amendment introduced in the 1946 House of Delegates, the effect of which would be to increase the size of the Council and which therefore would call for the election of additional Councilors. In order to remove any possible ambiguity as to the effective date of such amendment, if passed, Doctor Askey requested that the Council set as the first order of business for the second meeting of the 1947 House of Delegates the consideration of two constitutional amendments introduced in 1946. On motion duly made and seconded, the Council so ordered.

#### 5. Financial.

(a) Reports of March 14, 1947, bank balances.

February receipts and expenditures and balance sheet as of February 28, 1947, were received.

- (b) On motion by Kneeshaw, seconded by Anderson, it was voted that U. S. Treasury  $2\frac{1}{2}\%$  bonds of 1966-1971 maturity be purchased with funds on hand.
- (c) A report by California Physicians' Service on the application of funds advanced by the C.M.A. to aid C.P.S in meeting additional expenses in community enrollment drives was received.

At this point, 5:50 p.m., the Council recessed until 9:30 a.m., March 16.

#### 6. Complete Service Bureau of San Diego:

Kenneth Young, executive secretary of the San Diego County Medical Society, outlined the moves made by Complete Service Bureau of San Diego to request acceptance of that organization by the Council of the C.M.A. and by Associated Medical Care Plans, Inc., of the A.M.A. Mr. Hunton presented the formal request of Complete Service Bureau for Council approval. After discussion it was moved by Cline, seconded by Green and unanimously voted that approval of Complete Service Bureau by the Council be denied.

### 7. Public Policy and Legislation:

Mr. Von T. Ellsworth, Research Director of the California Farm Bureau Federation, appeared before the Council and urged C.M.A. approval of Assembly Bill 1247, which would permit county boards of supervisors to make beds in county hospitals available to all residents of the county regardless of financial status. He recalled meetings held between Farm Bureau and C.M.A. representatives in former years on this subject and stated that an agreement was reached by these representatives in regard to legislation then pending (1940-1941) that either organization would notify the other of any departure in its then legislative program.

After full discussion, it was moved by Cline, seconded by Shipman and unanimously voted that the Council disapprove AB 1247, that the California Farm Bureau Federation be notified of this decision with a full explanation of the reasons for it; namely, that the hospital bed shortage could best be met through additional hospitals constructed by community effort or under the hospital district law and with financial help from federal and state governments.

Dr. Murray, Mr. Reed and Mr. Hassard discussed a long list of measures now before the Legislature and the recommendations of the Committee on Public Policy and Legislation were approved by the Council.

On motion by Cline, seconded by Anderson, it was voted that the Council go on record as not approving any legislation the full content of which is not known, that the Executive Committee be likewise put on record and the Committee on Public Policy and Legislation be so advised.

#### 8. California Physicians' Service:

Doctor C. L. Cooley and Mr. W. M. Bowman appeared before the Council and presented a report

showing the present C.P.S. deficit at \$120,996, or the equivalent of six days' income at current revenues. This compares with 19 days' deficit in March, 1946, 28 days in 1945, and 27 days in 1944. During this period, the operating costs of C.P.S. have been reduced from 19.5 per cent of revenues in 1944 to 19.0 per cent in 1945, 16.7 per cent in 1946, and 14.5 per cent in 1947. Membership has risen consistently during this period to a total at present of some 432,000.

Doctor Cooley also reported that professional relations of C.P.S. are at their best point since formation of the service. He presented a study of California incomes, showing that 57.2 per cent of the people are receiving annual wages below \$3,000.

Doctor Murray reported that the present membership of C.P.S., in excess of 400,000, would represent a big help in his legislative work.

On motion by Moody, seconded by Green, it was unanimously voted that the Council express to the Trustees and the administration of C.P.S. the appreciation of the Council for the splendid progress report submitted.

On motion by Kindall, seconded by Anderson, it was voted to request that the recommendations of the "Chandler Committee" be reported on by the administration of C.P.S. at the meeting of C.P.S. Administrative members.

On motion by Cline, seconded by Shipman, it was voted that it be the sense of the Council that the recommendation contained in the "Chandler Committee" report calling for a survey of the business matters and practices of C.P.S. has been fulfilled by the survey undertaken by McKinsey & Co.

#### 9. Palo Alto Clinic:

Doctors Bruck and Cline reported on conferences held by them with Dr. Donald Tresidder, President of Stanford University, with Doctor Russel Lee and with Doctor George Houck, health director of Stanford. There were read several letters. including one from Doctor Lee in which he suggested that the approval of physicians to treat Stanford students, where such physicians are not members of the Palo Alto Clinic, be placed in the hands of the Stanford dean rather than the health director. There was also a letter from Stanford University approving such a change. Doctor Kneeshaw read a letter from Doctor H. J. Lane of Palo Alto on behalf of Palo Alto physicians who are not members of the Clinic. After considerable discussion, it was agreed that Stanford University is satisfied with the quality of medical care now being received by the students, that the contract has been amended to eliminate most of the original objections on ethical grounds and that the Santa Clara County Medical Society has expressed itself as willing to approve the new contract as amended by the latest proposal to give the Stanford dean authority over the approval of physicians outside the Clinic membership. An original motion by McClendon, seconded by Shipman, was amended and was voted as follows:

RESOLVED, that, with the understanding that

the Palo Alto Clinic-Stanford University contract will be amended and carried out in conformity with the proposal made by Dr. Russel V. Lee under date of March 13, 1947 and the consent thereto expressed by officials of Stanford University, the Council of the C.M.A. does not consider such contract to be in violation of the principles of medical ethics and therefore approves such contract; and be it further

RESOLVED, that the Chairman of the Council use his good offices to urge the administration of Stanford University to insert information in its student manual and other publications which will not be prejudicial to the interest of physicians who are not members of the Palo Alto Clinic.

#### 10. Medical Society of the State of California:

There was discussion of the reports on Medical Society of the State of California which had previously been made to the Executive Committee and the analysis prepared by legal counsel at the request of the Chairman of the Executive Committee. Doctor Regan discussed the two-way function of M.S.S.C. in (1) carrying on an education campaign on malpractice among all physicians, and (2) assuring personal legal service to those members against whom suits or threats of suits were brought. He stated his belief that the first function was not being effectively carried on because not all members of the Association read the information supplied. He also stated that in 1940 he had expressed the belief to M.S.S.C. that the dues of that organization, at least in the Los Angeles area, were not being effectively expended and that the educational function should be carried on by the Association. In reply to a question by Doctor Cline, Doctor Regan stated that he favored the assumption of these medical defense functions by the C.M.A., with the understanding that the administration of these functions should be on a county level.

After this discussion, it was moved by Shipman, seconded by Regan and unanimously voted that the C.M.A. Committee on Medical Defense be instructed to prepare a plan in conjunction with legal counsel whereby the services now provided by the Medical Society of the State of California could be furnished to all members of the California Medical Association.

#### 11. Public Relations:

Mr. Whitaker reported on the current legislative situation and the prospects of defeating proposals inimical to sound medical practice. He also reported on the progress of enrollment campaigns for voluntary health insurance. On motion by Cline, seconded by Kindall, it was voted that Mr. Whitaker plan at least one year ahead on a proposed C.M.A. public relations campaign and be prepared to discuss his plans with the Council and the House of Delegates at the 1947 annual session.

#### 12. Advisory Planning Committee:

Mr. Hunton reported on a meeting of the Advisory Planning Committee on March 15, 1947, with representatives of Mr. Whitaker's office in an

effort to secure greater effectiveness from the Voluntary Health Insurance Weeks planned for the metropolitan areas. He stated that this meeting had resulted in an agreement that such campaigns would be individually drawn up for the metropolitan areas and would thereby make the campaigns more effective.

#### 13. New and Miscellaneous Business:

(a) The Chairman read a letter from Doctor Hugh T. Jones asking that he be relieved of duties on the C.P.S. fee schedule committee and suggesting that Doctor John G. Manning of Pasadena be named in his place. With the consent of the Council, the Chairman suggested this change be made.

(b) On motion by MacDonald, seconded by Anderson, it was voted that the committee on Industrial Accident Commission fee schedules should meet at the time of the Annual Session and that members be invited to appear and offer suggestions for changes in the existing fee schedule.

(c) The Chairman announced and the Council approved the appointment of Doctors Frank A. MacDonald, H. Gordon MacLean and C. V. Thompson as representatives of the C.M.A. on an advisory committee on hospitalization to the State Department of Public Health.

#### 14. Next Meeting:

It was agreed that the next Council meeting should be at 12 noon on Tuesday, April 29, 1947, at the Hotel Biltmore, Los Angeles.

#### 15. Adjournment:

The meeting was adjourned at 5:30 p.m.

## Your Secretary and Editor Visit C.P.S. Offices

By L.H.G. AND D.L.W.

Quite recently we spent several hours visiting with the administrators of California Physicians' Service. Our visit included a tour of the C.P.S. offices, where we had opportunity to see the operations that are entailed in the complex business of bringing prepaid medical service to the people of California.

We began our tour where the new groups originate—the Sales Department—and followed the new members' association with C.P.S. completely through the organization.

In the Sales Department we were shown the sales literature, which describes the benefits that are available under the medical and surgical contracts. We were told about the comprehensive sales program whereby each month between twenty and thirty thousand new members are brought into the ranks of voluntary health coverage supporters.

From the Sales Department, we followed the applications of the new members into the Enrollment and Cashiering Departments. While there, we watched the applications being inspected and assigned the distinctive numbers which will hence-

forth identify the beneficiary in the files of C.P.S., and in doctors' offices, hospitals and laboratories throughout the state. In this same department, another group of employees was concerned with the job of collecting dues from some 2,500 different groups in Northern California.

Our next stop was the I.B.M. (International Business Machines) room. Here, noisy but efficient mechanical sorting and analyzing machines operate at high speed. In this department also (simultaneously with the identification card printing) a card is cut for a special file called "Positive Identification." This special file is maintained in order that each beneficiary member's history with C.P.S. can be secured at a glance. Special coding, read by trained personnel, furnishes the inquirer with such information as: type of contract held, payment or non-payment of dues, whether the established waiting periods have been completed, etc. This file is used principally for immediate identification when a doctor or his secretary calls in for a check on eligibility.

Now the preliminary registration work has been completed, and outside of the routine billing and collection procedures, C.P.S. has little or no further contact with the member . . . until he needs medical attention.

The beneficiary's next contact with C.P.S. comes through the physician he chooses from the list of over 7,800 who are participating in the program.

Our next stop then, was the Medical Claims Department. This is the place where the doctor's statement for services rendered (submitted on the regular C.P.S. forms) is priced from the fee schedule. We were told that about 80 per cent of the claims received could be classified as routine, and therefore could be handled by the pricing clerks. The remaining 20 per cent require the attention of the Medical Director or the Assistant Medical Director.

The claims are priced, audited and then sent to the statistician. It is here that invaluable records are being compiled which add strength to the foundation upon which prepaid medical service is being constructed.

Valuable statistics are being compiled here, also, which within a few years will be of inestimable value to the economics of medicine. From these files, investigators will be able to study thousands of case records.

Our question at this time, after seeing the thousands of medical claims being processed, was: "How do you keep your physician members up to date on these rapid developments in the program?"

We found the answer in our last stop. The Professional Relations Department. Here we saw forms being sent out to replenish the supplies in doctors' offices throughout all of Northern California. Since this was only the northern operation, a similar department is in operation in the Los Angeles office. We examined the huge rotary files that house the names and specialties of all of the member physicians. These files are used to compile the new lists of physician members, and to refer, on a rotating basis, veterans

who fall under the provisions of the C.P.S.-Veterans' Adminstration contract. We were introduced to some of the employees who call at the offices of participating physicians and keep them up to date on all phases of the refinements of the program. Although this seems like a monumental task, we were told that nearly 6,000 physicians' offices were personally contacted during 1946.

It was an impressive tour—one which showed us that selling and operating a state-wide prepaid medical service plan is a complex but deeply interesting job. And we were convinced that in our own state, our own C.P.S. is doing it in a way that should make each of us who are participating physicians proud of the part we are playing in its development.

## **Proposed Amendments To C.M.A. Constitution**

(SECOND PUBLICATION)

Second publication of two resolutions to amend the Constitution of the California Medical Association, which were introduced in the House of Delegates at the 1946 annual meeting, is made herewith:

#### RESOLUTION

Be It Resolved, That Section 12 of Article X of the Constitution of the California Medical Association is hereby repealed.

#### RESOLUTION

Resolved, That the Constitution of the California Medical Association shall be amended:

- 1. By deleting from Article VII, Section 1, Paragraph 4, the words, in line 6 thereof, "or more";
- 2. By adding to Article VII, Section 1, Paragraph 4, at the end thereof, the words, "and provided further that when any one councilor district shall have more than 1,500 members, one additional councilor-at-large for each additional 750 members or major fraction thereof shall be elected from its membership";
- 3. By adding to Article X, Section 1, Paragraph 1, at the end thereof, the words, "plus the additional councilors-at-large, as provided herein, in Article VII, Section 1";
- 4. By adding to Article X, Section 6, Paragraph 1, at the end thereof, the sentence, "Additional councilors-at-large, as provided herein, shall be elected each year when a vacancy exists or is created by increased membership in a councilor district"; and
- 5. By changing Article X, Section 9, Paragraph 3, thereof, to read as follows: "When a component county society shall have fifteen hundred members two of the councilors-at-large shall be elected from

its membership; and when a component county society shall have more than 1,500 members, one additional councilor-at-large for each additional 750 members or major fraction thereof, as herein provided, shall be elected from its membership. The district councilor and two of the councilorsat-large shall be elected in different years in calendar sequence. The additional councilors-at-large shall be elected as herein provided."

## In Memoriam

CASEY, TIMOTHY JOSEPH. Died from a heart attack, at Oakland, February 10, 1947, age 58. Graduate of the Creighton University School of Medicine, Omaha, Nebraska, 1916. Licensed in California in 1921. Doctor Casey was a member of the Alameda County Medical Association, the California Medical Association, and a Fellow of the American Medical Association.

COOK, CLARENCE WEINY. Died after a brief illness, at Los Angeles, March 5, 1947, age 71. Graduate of the University of Southern California School of Medicine, Los Angeles, 1908. Licensed in California in 1908. Doctor Cook was a member of the Los Angeles County Medical Association, the California Medical Association, and a Fellow of the American Medical Association.

DEERING, WALTER EVERETT. Died at Los Angeles, March 8, 1947, age 70. Graduate of the University of Southern California School of Medicine, Los Angeles, 1902. Licensed in California in 1902. Doctor Deering was a member of the Los Angeles County Medical Association, the California Medical Association, and a Fellow of the American Medical Association.

Green, Ray Carr. Died at San Bernardino, on January 16, 1947, age 47. Graduate of Northwestern University Medical School, Chicago, Illinois, 1928. Licensed in California in 1929. Doctor Green was a member of the San Bernardino County Medical Society, the California Medical Association, and a Fellow of the American Medical Association.

LOCKWOOD, MYRTLE SPENCER. Died after a two months' illness, at National City, California, on February 5, 1947, age 70. Graduate of the American Medical Missionary College, Battle Creek, Michigan, and Chicago, Illinois, 1900. Licensed in California in 1901. Doctor Lockwood was a Retired Member of the San Diego County Medical Society and the California Medical Association.

PRAY, RALPH EDGAR. Died of a brain tumor, at San Francisco, on December 18, 1946, age 50. Graduate of the University of Pennsylvania School of Medicine, Philadelphia, 1925. Licensed in California in 1941. Doctor Pray was a member of the Monterey County Medical Society, the California Medical Association, and a Fellow of the American Medical Association.

PRESTON, ADDISON WEBSTER. Died of uremia, at Visalia, on February 5, 1947, age 63. Graduate of the University of Vermont College of Medicine, Burlington, 1907. Licensed in California in 1909. Doctor Preston was a Retired Mem-

ber of the Tulare County Medical Association and the California Medical Association.

PRIEN, ROLAND HENRY. Died of a heart ailment, at Gilroy, January 23, 1947, age 66. Graduate of the University of Colorado School of Medicine, Denver, 1919. Licensed in California in 1920. Doctor Prien was a Retired Member of the Santa Clara County Medical Association and the California Medical Association.

SWIRE, FRANK PAUL. Died of injuries received in an airplane accident, at Santa Rosa, December 25, 1946, age 36. Graduate of the University of Colorado School of Medicine, Denver, 1940. Licensed in California in 1941. Doctor Swire was a member of the Sonoma County Medical Society and the California Medical Association.

TARNUTZER, BENJAMIN CHARLES. Died of a heart attack, at Los Angeles, on November 11, 1946, age 69. Graduate of Western Reserve School of Medicine, Cleveland, Ohio, 1902. Licensed in California in 1920. Doctor Tarnutzer was a Retired Member of the Los Angeles County Medical Association, the California Medical Association, and an Affiliate Fellow of the American Medical Association.

THOMASON, GEORGE. Died of a heart attack, at Los Angeles, on March 10, 1947, age 74. Graduate of Jefferson Medical College of Philadelphia, Pennsylvania, 1899. Licensed in California in 1901. Doctor Thomason was a Retired Member of the Los Angeles County Medical Association, the California Medical Association, and an Affiliate Fellow of the American Medical Association.

### **Dr. George Thomason**

Dr. George Thomason, for many years one of the foremost surgeons on the Pacific Coast, died on March 10, 1947, in Los Angeles, California. Dr. Thomason was born in Camden, New Jersey, on November 6, 1872.

He attended college in Battle Creek, Michigan, and later began the study of medicine in the American Medical Missionary College. He completed his undergraduate medical education at Jefferson Medical College in Philadelphia, where he received his degree of doctor of medicine in 1899. Specializing in surgery, he became assistant surgeon at the Battle Creek Sanitarium; and in 1904, having received a diploma as Licentiate of the Royal College of Physicians and Surgeons in Dublin, Ireland, he accepted the position as medical director of the Cape Sanitarium in Capetown, South Africa, where he spent the following seven years.

Returning to the United States in 1911, he became the superintendent of the St. Helena (California) Sanitarium, and in 1914 came to Los Angeles, where he entered the private practice of surgery, and at the same time became professor and head of the department of general surgery in the College of Medical Evangelists. He held this position until the time of his death. Since 1915 he

had been chief of the surgical staff at the White Memorial Hospital, and had served in a similar capacity at the Los Angeles County Hospital.

He was also consulting surgeon to the Southern Pacific Railroad Company, the Glendale and Loma Linda Sanitariums, and the Los Angeles Police Department. Since 1934 he had been a member of the Board of Medical Examiners of the State of California.

He was a Fellow of the American College of Surgeons, was certified by the American Board of Surgery, and was a member of the American Medical Association, the California State and Los Angeles County Medical Associations, the Western Surgical Society, and the Los Angeles Academy of Medicine.

Tennis and fishing were his chief recreations, and for many years he was an active member in the Los Angeles Tennis Association.

Dr. Thomason was a man of high moral character, was greatly admired by his friends and patients, and was a teacher of unusual ability.

He is survived by his widow, Mrs. Enanora Thomason, and by his daughter, Kathryn, who is the wife of Dr. Archie A. Steele of Los Angeles.

### **House of Delegates Meetings**

First meeting of the C.M.A. House of Delegates is scheduled for Wednesday, April 30 at 4:30 p.m., NOT the afternoon of May 1 as shown in the March issue of California Medicine. The second meeting will begin at 4:30 p.m. Friday, May 2. Both meetings will be in the Music Room,

## NEWS and NOTES

#### NATIONAL • STATE • COUNTY

#### LOS ANGELES

Dr. George D. Wells has replaced Dr. Harry F. Becker as health officer of the City of Vernon, Los Angeles County.

James J. Short, M.D., formerly of New York City, who for many years was associated with the New York Postgraduate Medical School and Hospital, has been appointed to the faculty of the College of Medical Evangelists as associate professor of Medicine. He is director of the basic science course in Internal Medicine offered by the Graduate School of Medicine.

The College of Medical Evangelists Graduate School of Medicine, Los Angeles, announces the offering of courses on a full-time basis in the basic sciences and their clinical application, to graduate students in Internal Medicine, General Surgery, Obstetrics and Gynecology, Otolaryngology, and Urology, October 1, 1947, to June 11, 1948. Parttime postgraduate courses are also offered from time to time through the year. Further information may be had from the Dean, Graduate School of Medicine, 312 North Boyle Avenue, Los Angeles 33.

Dr. Leroy B. Sherry, Pasadena physician, was recently elected president of the Pacific Coast Surgical Association. Dr. Sherry, who served as vice-president of the Association last year, was elected president for the coming year at the group's annual five-day conference in Seattle and Victoria, British Columbia.

Dr. Nathaniel Berman, who during the war was attached to the U.S. Army Medical Corps, has opened offices at 5330 Lankershim Blvd., North Hollywood. Dr. Berman is an eye physician and surgeon.

Dr. J. M. Furstman has been named head of the Santa Monica District Health Office to succeed Dr. W. F. Reasner, who retired March 1. Dr. Furstman was head of the Health Office at Monrovia for 24 years.

"Shall the Government Practice Medicine?" was the topic for a talk given recently by **Dr. E. T. Remmen**, president of the Los Angeles County Medical Society, before the Burbank Optimists Club. Dr. Elmer Zeiss was program chairman.

Dr. Lowell S. Goin, president of the Board of Trustees of California Physicians' Service and past president of the California Medical Association, was guest speaker at a recent Rotary Club luncheon in Glendale. His subject: "Health Insurance and the Nation."

#### NAPA

Major George T. Pomeroy, formerly chief surgeon at the Veterans Home, has retired at the age of 70. Dr. Pomeroy, who has been a member of the Home medical staff since 1933, is now on terminal leave recovering from an operation.

#### SAN DIEGO

San Diego County has increased the salaries offered for four positions in the County Hospital which it is seeking to fill, and at the same time has extended the time for receiving applications for the posts. The positions and the salary range: Pathologist, up from a range of \$483-530 per month to a range of \$559-616; Radiologist same as Pathologist; Physician Anaesthetists up from \$460 per month to \$532; Medical Director TB up from \$587 per month to \$532; Medical Director TB up from \$587 per month to \$647. Filing time for applications has been extended to May 12, 1947. Application forms are available from Mrs. Marie B. Cook, Department of Civil Service and Personnel, 212 Civic Center, San Diego.

The San Diego County Medical Society's business and administrative activities have been moved into new offices at Room 101, Medico-Dental Building, San Diego. The San Diego County Branch, California Division, American Cancer Society also occupies space with the Medical Society.

Dr. Clark M. Johnson, Associate Clinical Professor of Urology, University of California Medical School, spoke at the regular March scientific meeting of the County Society on "Difficulties in the Early Clinical Recognition of Hydronephrosis."

#### SAN FRANCISCO

Dr. Frederick C. Cordes, clinical professor of opthalmology at the University of California, recently delivered the third annual Sanford R. Gifford Memorial Lecture to the Chicago Opthalmological Society.

A distinguished doctor in the field is chosen each year for the lecture in honor of the late Dr. Gifford, who was a member of the faculty at the Northwestern Medical School in Chicago.

An Eye Bank-a central registry through which healthy corneas may be obtained for transplanting into the eyes of persons blinded because of damaged corneas-has been set up by Stanford University in the Stanford University Hospital, San Francisco. Like eye banks already operating in New York, Boston, and Chicago, the Stanford bank will have as its functions the registry, collection, preservation and swift transportation of donated eyes so that they will be available for use by qualified eye surgeons on the Pacific Coast. Arrangements for swift transportation, which is necessary because of rapid deterioration of the tissue once it is removed from the donor, have been made with airlines, railroads and bus lines. Sources of corneas for transplantation are eyes removed from living persons because of injury or disease which has left the cornea undamaged, and eyes removed soon after death.

New appointment of two professors and promotion of 19 members of the faculty of **Stanford University School of Medicine** was announced last month by Donald B. Tresidder, president of the University.

Dr. Charles E. McLennan, professor and head of the department of obstetrics and gynecology at the University of Utah School of Medicine, was named to a similar position at the Stanford School of Medicine in San Francisco.

Dr. Josephine R. Hilgard, director of the child guidance clinic at Children's Hospital in San Francisco, was appointed associate clinical professor of medicine.

Dr. William H. Northway was promoted to an associate professorship in medicine. Other promotions: To clinical professorships-Dr. Garnett Cheney. in Medicine, Dr. Ann Peril Purdy, in Pediatrics: To Associate Clinical Professorships-Dr. John Wesley Cline, in Surgery, Dr. Robert Scarborough, in Surgery; To Assistant Clinical Professorships-Dr. Henry Dean Brainerd, in Pediatrics, Dr. John Ford Card, in Medicine (Neuropsychiatry), Dr. Chester L. Cooley, in Obstetrics and Gynecology, Dr. Francis Cox, in Surgery (Bone and Joint), Dr. Frederick Fender, in Surgery, Dr. Frank Gerbode, in Surgery, Dr. Lot D. Howard, in Surgery, Dr. Frank Lusignan, in Surgery, Dr. Willard M. Meininger, in Medicine, Dr. Walter Work, in Surgery (Otorhinolaryngology); To Clinical Instructors—Dr. Edward C. Defoe, Jr., in Pediatrics. Dr. Kalmen Klinghoffer, in Medicine, Dr. Robert Lee Smith, Jr., in Medicine, Dr. Philip R. Westdahl, in Surgery.

#### SAN JOAQUIN

Discharged from the Navy in October, Dr. Henry C. Rixford has opened offices in the Flor Building, 2013 Pacific St., Stockton. Dr. Rixford formerly practiced in Stockton from 1934 until 1939, when he moved to Sonora. While in the Navy, he was in charge of the orthopedic ward at Treasure Island Hospital.

#### **VENTURA**

**Dr. Donald P. Musgrave,** who has been practicing in Fillmore for almost a year, left recently for Washington, D. C., where he will study dermatology for three years. He then plans to return to practice in Ventura County.

#### GENERAL

The 13th Annual Meeting of the American College of Chest Physicians is scheduled to be held at the Ambassador Hotel, Atlantic City, New Jersey, June 5 to 8. The oral and written examinations for Fellowship will be held on the first day of the meeting, June 5. Applicants for Fellowship in the College who plan to take these examinations should communicate now with the Executive Secretary, American College

of Chest Physicians, 500 North Dearborn Street, Chicago 10, Illinois.

Five physicians have recently been added to the staff of the California State Department of Public Health. Dr. George T. Palmer, Consultant in Public Health Administration, Division of Administration, has come to the department following an assignment with the United States Public Health Service. Dr. J. Walter Hough, Medical Officer, Bureau of Adult Health, is on loan from the U. S. Public Health Service. Before joining the department he served with the Oklahoma Health Department. Dr. Marion Iosephi, Consultant in Rheumatic Fever, Bureau of Maternal and Child Health, has had wide experience in children's cardiac clinics and hospitals in this country and abroad. She served with the U. S. Navy immediately before her appointment to the California post. Dr. Joseph A. Moore, Acting Chief, Acute communicable Disease Service, takes up his duties following special work on the department's blood bank study which he recently completed for the Division of Laboratories. Dr. Yoshiye Togasaki, Medical Officer, Bureau of Maternal and Child Health, will assist in the administration of the Emergency Maternity and Infant Care and the crippled children's programs. She served with U.N.R.R.A. and was in charge of displaced persons camps in southern Italy during the war.

The American Academy of Allergy, in cooperation with the Medical Faculty of the University of California, will offer an Orientation course in Clinical Allergy for General Practitioners at the University of California Hospital, San Francisco, from July 7 to 11 inclusive, 1947, under the auspices of Medical Extension, University of California. Details of the course (which has received the approval of the Committee on Education of the American Academy of Allergy) will be announced later.

Rules governing the annual award of the \$200 "Foundation Prize" of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons for the best pertinent manuscript of 5,000 words or less have been set up by the association. Copies may be obtained from James R. Bloss, M.D., Secretary, 418 Eleventh Street, Huntington, W. Virginia.

An intensified student nurse enrollment program will be conducted on a nationwide scale by the American Hospital Association throughout 1947, according to announcement by John H. Hayes, Association president. In an effort to overcome the acute shortage of nurses, the association plans direct aids to hospital schools of nursing with a backdrop of national publicity, Mr. Hays said. The Association's Board of Trustees voted an expenditure of 10,000 for the campaign, and hospital schools of nursing and other organizations affected by the shortage of nurses are being asked to contribute financial help.



## INFORMATION

# The Poliomyelitis Coordinating Council's Role in the 1946 Epidemic in Los Angeles\*

California's experience with poliomyelitis in 1946 had two interesting aspects: first, the concentration of cases in one area, Los Angeles; and, second, the manner in which that community mobilized its resources to meet the epidemic.

Of 2,166 cases reported during the year in the state as a whole, 1,306 were located in Los Angeles County. The sharpness of the epidemic becomes even more apparent when one considers that 1,014 cases occurred in Los Angeles County during the ten-week period, July 28-October 11, 1946.

Early in August it was evident that an epidemic was impending. At the invitation of the State Department of Public Health, representatives from the County General Hospital, private hospitals, local chapters of the National Foundation for Infantile Paralysis, American Red Cross and Sister Kenny Foundation, County Medical Association, and the Los Angeles health departments formed a Poliomyelitis Coordinating Council.

Each of these agencies had a distinct contribution to make. The Council met periodically throughout the epidemic period in order to integrate their activities.

Acute cases were hospitalized during their quarantine period at the County General Hospital. Thereafter those requiring further hospitalization were transferred to facilities—both private and public hospitals—for convalescent care under the auspices of the National Foundation for Infantile Paralysis. The latter organization also secured needed equipment and subsidized the payment of personnel during the epidemic.

The American Red Cross, quickly meeting every quota set by the medical authorities, recruited over 200 nurses from several western states for service in the County General Hospital. In addition, there was special recruitment of physical therapy technicians, medical social service workers and "packers" by the County General Hospital and the National Foundation for Infantile Paralysis.

In order to assure continued medical supervision after hospital discharge, a follow-up system was established, utilizing the public health nurses of the health departments as well as the medical social services of the hospitals.

Organization of a Poliomyelitis (Preparedness)
Coordinating Council before an epidemic strikes
would no doubt minimize the problems which

arise during an epidemic. Particularly in larger cities such a council appears justifiable in view of the relative complexity of community organization.

In planning to meet an epidemic of poliomyelitis, attention should be given to the following items: bed space (both acute and convalescent), equipment, personnel, publicity, discontinuing nose and throat surgery, and a follow-up system. In the case of recruited personnel provision should be made for transportation, physical examinations and medical care, housing, training and supervision on the job, and clear cut financial arrangements.

#### **Coming Medical Meetings**

American Association of Industrial Physicians and Surgeons, Buffalo, N. Y., Statler Hotel, April 26-May 4. Address: Dr. Frederick W. Slobe, 28 East Jackson Boulevard, Chicago 4, Secretary.

American College of Chest Physicians, Atlantic City, N. J., Ambassador Hotel, June 5-8. Address: Executive Secretary, American College of Chest Physicians, 500 North Dearborn Street, Chicago 10, Illinois.

American College of Physicians, Chicago, April 28-May 2. Address: Mr. E. R. Loveland, 4200 Pine Street, Philadelphia 4, Secretary.

American Congress of Obstetrics and Gynecology, St. Louis, September 8-12. Address: 24 West Ohio Street, Chicago 10, Illinois.

American Society for Clinical Investigation, Atlantic City, Chalfonte-Haddon Hall, May 5. Address: Dr. Eugene A. Stead, Jr., Grady Hospital, Atlanta 3, Georgia, Secretary.

American Society for Research in Psychosomatic Problems, Atlantic City, May 3-4. Address: Dr. Edwin G. Zabriskie, 714 Madison Ave., New York 21, Secretary.

American Society for the Study of Sterility, Atlantic City, N. J., June 7-8. Address: Dr. John O. Haman, 490 Post Street, San Francisco 2, California.

Association of American Physicians, Atlantic City, May 6-7. Address: Dr. Joseph T. Wearn, Lakeside Hospital, Cleveland 6, Secretary.

California Medical Association, Los Angeles, Hotel Biltmore, April 30-May 3. Address: Dr. L. Henry Garland, 450 Sutter Street, San Francisco 8, Secretary.

<sup>\*</sup> From the California State Department of Public Health.

# Letters to the Editor . . .

## CANCER AND THE EMBRYONAL HYPOTHESIS

One of the oldest and yet most persistent theories of cancer genesis is the embryonal one. As early as 1829 Lobstein and Recamier compared the growth of tumors to that of embryonal tissue. In 1854 the embryologist Robert Remak first proposed the theory that cancer as well as certain benign tumors arose from groups of misplaced somatic cells comprising embryonic "rests" or residues. Some years later Julius Cohnheim adopted the theory, and largely through his influence it gained wide and lasting currency. Historically, then, the "Cohnheim theory" is more accurately described as the "Remak-Cohnheim theory."

The theory of embryonic rests came as a logical consequence of the universal acceptance of Kaspar Friedrich Wolff's thesis of epigenesis, which completely supplanted the preformationist theories of the ovulists and homunculists. The proponents of epigenesis reasoned that if embryogenesis does not involve the unfolding and expansion of a preformed organism, then the development of an organism from the egg must involve the gradual adding of part-to-part much in the same manner that a house is assembled from a mass of bricks. What is more natural, they reasoned, than that some of these "bricks" be misplaced in the process of building?

The mechanistic aspect of this literal interpretation of epigenesis became apparent when examined in the light of Hans Spemann's researches, published in 1900, on organizer action and embryonic induction. Spemann showed that the surface ectoderm of any part of the early embryo when placed over the optic vesicle underwent lens induction. Others have since been able to duplicate this induction phenomenon through the use of a number of various chemicals.

Experiments of the nature of Spemann's have since been multiplied an hundredfold. Data from thousands of other transplantations in experimental embryology may be summarized as follows: (1) when a piece of embryonic tissue that has not yet been determined or differentiated into a specific organ type is transplanted into another organ field. the transplant differentiates in conformity with the morphological pattern of the host organ; (2) when a piece of embryonic tissue is transplanted after determination, it differentiates at the transplanted site in conformity with the morphological pattern of the site from which it was derived. Since any hypothetical misplacement of embryonic cells would necessarily occur very early in development, such cells would differentiate according to the tissue in which they were misplaced; hence they could form no so-called embryonic rests.

Oberling has summarized the case against the embryonal hypothesis of carcinogenesis very well: "It is true that embryonal cells do somewhat re-

semble cancer cells in appearance, but the two are entirely different in nature. For whereas the proliferative vigor of the former gradually flags as they differentiate to form normal tissues, their malignant prototypes continue to multiply indefinitely and end at last in anarchy and ruin.

"But, it may be said, in the embryo growth is restricted by controlling and directing influence; in the body of the adult, where these are missing, the embryonal cells behave quite differently. Experiment does not confirm this objection. Embryonal tissues in all stages of development have been inoculated into countless adult animals, and always with the same outcome; they never changed their character, but continued to act as they do in the embryo, growing for a time but ending as mature tissue."

Although the cancer cell is not embryonic, neither is it a spontaneously created component of the lifecycle. As Virchow pointed out long ago, no morbid process can evoke from a cell or cells potentialities that are not inherent. The cancer cell has its normal counterpart in the animal life-cycle, and this counterpart is the non-embryonic trophoblast cell of the early conceptus. The trophoblast cells develop before the definitive embryo, form no part of the definitive embryo, and may persist after the embryo is gone. The trophoblast cells arise as a result of the initial cleavage of a gametogenous cell that in turn has arisen from the meiosis of a diploid totipotent cell. Although inadequacies in earlier terminology have obscured the fact, the trophoblast cell is the very antithesis of the embryonic cell, and will destroy definitive embryonic cells in a malignant fashion when cultured with them in vitro. The malignancy of the normal trophoblast cell, removed from the checking influence of the mother, is not exceeded by any known exhibition of cancer.

While the facts of modern embryology dispose of the embryonic theory of cancer by disposing of embryonic rests, modern embryology recognizes the migration of specific non-embryonic cells during embryonic development: these cells are the diploid totipotent cells that comprise the morphologically continuous line of germ-cells that extend from generation to generation. A great number of workers have proved the migration and ectopic dispersion of these cells in animals and in man. The diploid totipotent cells that enter the normal canalization of the gonads must undergo meiosis to produce functional gametes. The division of a gametogenous cell so produced can occur only by the initial production of trophoblast, which marks the earliest stage of the conceptus. If the production of trophoblast occurs through the meiosis of an ectopic totipotent cell, the resulting trophoblast is either destroyed or exhibited as cancer—the most malignant exhibition of which consists of the frank trophoblast cells of extra-genital chorionepithelioma. As we have frequently emphasized, a trophoblast cell has *never* been observed in the male except as the most malignant exhibition of cancer—nor so in the female outside of the canalization of

pregnancy.

There is no known property of the cancer cell which is not possessed by the trophoblast cell. Trophoblast cells in every respect indistinguishable from those of normal pregnancy comprise the most malignant exhibition of cancer: chorionepithelioma. Primary chorionepitheliomas have been found extra-genitally in both sexes (thus again proving the ectopic presence of the parent totipotent cell), and some of the trophoblast cells comprising these tumors have been exhibited as adenocarcinoma or sarcoma in metastases. In examining over 900 cases of testicular tumors, Friedman and Moore found the majority of them to contain frank cellular and syncytial trophoblast. In some cases the trophoblast was overt only in metastases, in other cases only at the primary site, and in many cases in both sites.

Like many other ideas in science that have been favorably received over several generations, the thesis of the so-called embryonic nature of cancer and the idea of embryonal rests are thus not entirely without justification. The so-called lost cells are the totipotent migrating germ-cells and the so-called embryonal cells are the trophoblast cells. This parallelism, however, cannot mitigate the urgency for the strictest precision in our terminology on the subject of growth and development.

Although it is not possible to attempt here an outline of the evidence for the trophoblastic nature of cancer, this is the only thesis of carcinogenesis for which not a single tenable theoretical or experimental contradiction has ever been found. A wealth of positive data exists for the support of the tropho-

blast thesis.

It is true that somatic cells and tissues are sometimes found in anomalous positions, but this is the result of anomalous organizer action on highly competent or undifferentiated cells-and not the result of their mechanical transposition. Just as the osseous tissue that sometimes can be induced in skin by the prolonged application of methylchloranthine is due, not to mechanically displaced bone cells but to the anomalous organizer effect exerted by the chemical on highly competent cells, so the whole phenomenon of carcinogenesis - according to the trophoblast thesis—has as its basis organizer phenomena which involve exclusively the meiosis of a totipotent cell with the consequent evocation of the pleomorphic trophoblast cells that (however masked morphologically by the tissue field in which they find themselves) form the constant malignant component of all exhibitions of cancer.

#### REFERENCES

Friedman, N. and Moore, R.: Military Surg., 99(5):573-

Krebs, E., Calif. Med., 65:261-262 (Nov.), 1946.

Oberling, C.: "The Riddle of Cancer" (trans. by Wm. Woglom), Yale University Press, New Haven, 1944, p. 31. Remak, Robert: Deutsche Klink., 6:170, 1854. Spemann, H.: "Embryonic Development and Induction," Yale University Press, New Haven, 1938.

ERNEST T. KREBS, Division of Anatomy, University of California Medical School, San Francisco 22.

#### REHABILITATION OF TUBERCULOUS PATIENTS

I note a very liberal quotation in California Medicine, November, 1946, issue; Vol. 65, No. 5, page 58, quoting from the current issue of *Hygeia* on "Rehabilitation of Tuberculous Patients" by Joseph B. Rosner, M.D., of the National Jewish Hospital, Denver, Colorado.

I should like to take exception to point No. 5 in this program. As far as the patient is concerned, this is really the key point in all of those that are mentioned. I am quite sure that it is not current opinion among experienced phthisiologists that "it is not wise for a patient to return to the occupation in which he was engaged before becoming ill." I believe, in general, that the advice given is exactly the reverse of this, unless the occupation is definitely unsuitable—which holds true for persons doing heavy manual labor or those exposed to a silica hazard. I know the general composition of the patients in the National Jewish Hospital in Denver, and I am sure this is not good advice for them.

This point, I feel, is very important. Many patients, as well as a number of doctors, will undoubtedly read this article, and may be influenced by it. Hygeia is generally a very reliable publication. I believe that some step should be taken to confirm my opinion, and a definite effort made to counteract the unfavorable advice which will be given, I am afraid, to many patients on the basis of this statement.

Sincerely yours,
H. G. TRIMBLE, M.D.,
419 Thirtieth Street,
Oakland 9, California.



## **BOOK REVIEWS**

AN INTEGRATED PRACTICE OF MEDICINE—A Complete General Practice of Medicine from Differential Diagnosis by Presenting Symptoms to Specific Management of the Patient. By Harold Thomas Hyman, M.D., Volumes I. II, III, and IV, and Index. 1184 illustrations, 305 in color. 319 Differential Diagnostic Tables, Philadelphia and London. W. B. Saunders Company, 1947. Price \$50.00 per set.

At the end of a preface eight and a half pages in length Dr. Hyman writes the following 97 word sentence: "If 'An Integrated Practice of Medicine' fulfills the requirements for which it has been devised, it should be possible for the practitioner, after taking the history and performing the physical examination, to turn to the Index of Differential Diagnosis, obtain a reference to the needed Tables of Differential Diagnosis, establish a definitive diagnosis or be guided to additional examinations and tests by which the diagnosis can be established; and then prepare a therapeutic routine to include symptomatic, specific and prophylactic therapy for the relief or cure of the abnormal manifestation concerning which his patient has consulted him." Surely no writer has ever set himself a more pretentious task in a more pretentious fashion. If one is to believe the author or the advertising matter of the W. B. Saunders publishing company or even the medical editor of Time magazine, the author has fully succeeded in this task.

Despite the weight of such authority we refuse to be stampeded into so complete an endorsement. The author has gone mining for gold. He has struck pay dirt, but the ore varies widely in quality. There are many excellent things about the book: A tremendous mass of information is presented in a generally up-to-date manner. The indexing, found separately at the end of each volume and in a separate volume for the entire work, is altogether admirable. The cross-indexing throughout the four volumes ties them together more inextricably than any other lengthy work with which the reviewer is acquainted. The photographic illustrations are numerous and generally good.

"Integrated Practice" is a medical almanac, chuck-full of all kinds of medical information. Although quite a number of co-authors cooperated in the writing of different sections, one has to look too diligently to find the acknowledgment of their work (at the beginning of the section or of the book). It is unlike the average almanac in that the dominating personality of the senior author keeps interrupting the facts with his opinions and keeps substituting his philosophy for techniques. He has certain concepts not universally accepted by the general body of medical authority and utilizes a textbook to spread his doctrines.

Except for the illustrations there are very few acknowledgments of source material or of original work, no matter how recent. It is felt that a short number of references to recent work would be desirable at the end of each chapter.

The tables of differential diagnosis are numerous and cover a vast field. They are not constant in their relation to the principal subject involved. For example, the table on Tympanites comes on page 1878 after the discussion on intestinal obstruction. But on page 1880 the table on Pain in the Right Lower Quadrant is presented before the discussion of acute appendicitis. The tables are not as uniformly inclusive as one might wish. The table on Pain in the Right Upper Quadrant does not list inflammations of the diaphragm, perihepatitis, Laennec's cirrhosis, or the fatty liver of alcoholism, which are surely more likely to be encountered by the general practitioner than hypertrophic cirrhosis of Hanot, the existence of which is questionable.

The senior author states that he himself has deliberately written the section on the Nervous System including Psychiatry in the belief that his exposition will meet the need of the practitioner better than that of an author with more formal training. The reviewer is compelled to the view that more knowledge is a larger argument than less training. The presentation on intracranial injuries (pages 1450 to 1455) is poor. The course and treatment of cerebral concussion are not clearly presented. The syndrome is discussed as a phenomenon of the prize ring. Automobile accidents, which are more common, are not mentioned. A dilemma is posed for the reader on page 1295. The author generalizes that "the treatment of coma cannot be carried out with intelligence until the causative factor is elucidated." But shortly afterward he specifies "if spinal fluid is turbid, temperature is elevated or leukocytosis is pronounced, inaugurate ... penicillin." It is bad that the pupil should use antibiotics without specific reason; it is worse that the teachers should advise this practice.

Certain other errors may be pointed out: On page 959 the statement is made "patent ductus, alone of the congenital cardiac lesions, is accessible to surgery." The published work of Taussig and Blalock on the surgery of cyanotic heart disease antedates this book by many months. The section on coccal infections (page 154) similarly omits mention of Romansky's development of penicillin in beeswax and oil and dogmatizes that if the patient is ambulatory, sulfonamides must be employed. In the discussion of acute appendicitis, anorexia is not mentioned as one of the cardinal symptoms and the statement is made dogmatically (page 1882) that "diarrhea does not occur unless the patient is . . . given a purge." Most surgeons will dispute this.

The Wintrobe method is not mentioned in measuring the sedimentation time of erythrocytes, but is listed immediately afterwards to measure the hematocrit. It is stated wrongly that the tube used requires 3 cc. of blood (instead of 1 cc.).

Most of the tests of liver function are discussed in a general way only. Yet certain tests, used relatively rarely, such as the galactose tolerance, are presented in detail. The technique for the bromosulphthalein excretion test recommends the injection of 2 mg. of the dye per kilo of body weight instead of the more generally accepted 5 mg. per kilo.

The training and the acumen of the radiologist are slurred. Diagnostic roentgenology is completed in the space of three pages. One receives the impression that the only films which need to be referred to the specialist are those of the nasal accessory sinuses, and that "any physician who has learned to operate a motor car and a radio set can learn clinical radiography with slightly greater effort."

At times the text is scholarly, at times very sketchy and even inaccurate. The reviewer doubts that this unevenness of presentation is deliberate. He suspects it may be due to the fact that the senior author is more conversant with some branches of medicine than with some others. He suggests that a second edition of the book might be made a more accurate Vade Mecum for the practitioner if various specialists, themselves with a broad general outlook, were given freer rein under the general editorship of the senior author. The general practice of medicine today covers so many subjects with so many details that no one man can master them all—and this fact may be acknowledged freely without loss of stature.

MENSTRUAL DISORDERS AND STERILITY. By Charles Mazer and S. Leon Israel. Second Edition. Completely revised. With 133 Illustrations. Paul B. Hoeber, Inc., Medical Book Department of Harper & Brothers, New York, London. Price \$7.50.

Mazer and Israel have written the second addition of "Menstrual Disorders and Sterility." It was written for students and practitioners, but it will be far more valuable to Endocrinologists and those specialists in Obstetrics and Gynecology who have a particular interest in the fields so adequately covered.

The first chapter describes in detail the various gonadotropins. In the second chapter the many uses of the estrogen, both natural and synthetic, are carefully discussed. Progestin and its effects are also carefully described. One is immediately impressed with the wide variation of dosages, effects and results, and it can not be said that this particular chapter will clarify in the minds of the average practitioner just what should be used, and when and how.

Dysmenorrhea, so often neglected in the average textbook, seems to be given a most complete discussion. Many of the therapeutic measures have been given in detail and the postural treatment as devised by Billig and Dick is given due and just consideration. Possibly some readers will feel that too much emphasis has been placed on the use of the endocrines.

The discussion of sterility is well presented, but again the use of the gonadotropins, estrogens and progestin may be too enthusiastically recommended. Special attention is given to the cervical factor in the barren patient, and this seems to comprise the most important portion of the authors' remarks on infertility.

Habitual abortion, as described under relative sterility, seems to show that the authors have brought the text of a rapidly increasing knowledge up to date, and the Rh factor, toxemia of pregnancy and the management of threatened abortion are most satisfactorily discussed.

The book has much to offer to the specialist, but it is probably a little too exhaustive and detailed for ready consumption by the practitioner.

A TEXTBOOK OF CLINICAL NEUROLOGY. By J. M. Nielsen, B.S., M.D., F.A.C.P., Associate Clinical Professor of Medicine (Neurology), University of Southern California; Senior Attending Physician (Neurology), Los Angeles County General Hospital; Attending Neurologist, Hospital of the Good Samaritan, Los Angeles, California. Second edition, revised. With 190 illustrations. Paul B. Hoeber, Inc., 'Medical Book Department of Harper & Brothers, New York City. Price \$7.50.

In an excellent text and reference book on Clinical Neurology, Dr. Nielsen's clear, concise style has allowed him to incorporate in a single volume an amazing mass of neurological data. Unlike the usual text book, this volume combines the essential neuro-anatomy and the symptomatology with the author's extensive clinical experience.

The second edition includes some revised chapters and some additional information of a newer character. This brings the text up-to-date, but this is of minor importance as compared to the manner of presentation of the fundamental syndromes essential to neurological diagnoses.

The chapters dealing with vascular and inflammatory lesions of the brain are excellent. However, the outstanding feature is the discussion of cerebral localization. Short, concise discussion is given of electroencephalography which is well worth reading in view of the extensive use which is being made of this diagnostic method at the present time.

Although classified as a text book of clinical neurology, it is likely that this volume will prove far more valuable as a ready source of reference. A complete source of neurological conditions for those interested not only in internal medicine but in neurology and neurosurgery as well.

HARVEY CUSHING, A Biography. By John F. Fulton. Copyright 1946. First edition, 150 illustrations. Charles C. Thomas, Publisher, Springfield, Illinois. Price \$5.00.

The story of Cushing's life is divided readily into four fairly distinct phases. The first is that of his formal schooling. It includes his graduation from Yale and the years in Harvard Medical School and Hospital up to the time of his departure for Johns Hopkins at the age of 27. Next comes the period of his surgical training and his preceptorship under Professor Halsted. These were the formative years in his surgical development and led to his appointment to the faculty. Then follows his assumption of the Moseley Professorship of Surgery at Harvard Medical School in 1912, and the post of Surgeonin-Chief at the Peter Bent Brigham Hospital in Boston, where he continued until his retirement in 1932 at the age of 63. The final years were spent at New Haven. These permitted devotion to his

bibliographic interests, and resulted in establishment of the medical library.

For the preparation of this biography abundant material was available to the author. Doctor Cushing, with characteristic foresight, anticipated and made provision for it. His own files of letters, notes, diaries, sketches and photographs were carefully kept, and these were supplemented by family, friends and associates. Correspondence, much of it from Cushing's own letters, is liberally transcribed. The choice of appropriate selections must have taxed the good judgment of the biographer.

His lineage is dealt with comprehensively. Letters to his parents and immediate relatives are numerous. His prolific letter writing, which seemed unusual in boyhood, persisted through life. His facility with the pen was not confined to writing, for his artistic ability was evident early and was marked in his college days. During this period his great energy, good coordination, and athletic ability were combined with a keen competitive spirit.

During his years of training at Baltimore and his long preceptorship he received the Halsted imprint and was well grounded in those surgical methods characteristic of the Halsted school. To these he adhered throughout life. All phases of his work, the preoperative studies and careful recording, the operative technique, from the meticulous preparation of the field of operation down to the final dressing, were those of "the Professor." In addition, the detailed and exhaustive character of Halsted's scientific contributions could not fail to afford to his pupil the best example of surgical writing. The biographer has dealt lightly with the place of Professor Halsted in the Department of Surgery of Johns Hopkins and in the field of surgery in the United States. It would seem that those acquainted with the Baltimore period of Cushing's life and work would be more apt to view Cushing as an able and receptive pupil in surgery who was given exceptional guidance and opportunities. His surgical methods were all in the Halsted pattern. The association with Osler and Welch and their interest were inspirations for the young surgeon. Fulton has viewed their relationship with him more as that of full contemporaries, as developed in later life.

In the twenty-year period in Boston, which began at the age of 43, Cushing is portrayed at the full development of his abilities and productivity. His numerous publications, his contributions, both scientific and literary, and his extraordinary and well-deserved honors are given in detail. His views on medical education and "full time" would be of interest to all teachers. Sufficient detail is given to be of greatest interest to surgeons and neurologists, but a nice balance is maintained and the interest of lay readers is held.

This book portrays a surgeon who has done more than any other to lead followers into this field. The surgery of neoplasms came to dominate his interest, rather than the broad field of neurological surgery, and most of his pupils have followed this lead. Thoroughness and meticulous attention to detail characterized his technical work, along with a tendency toward over-elaboration

rather than simplification. His literary abilities were not surpassed by any contemporary medical writer. They were partly the result of his native ability and early taste. It is an encouragement to those less gifted to realize the painstaking and frequent recasting and rephrasing which contributed to the style of his finished product. His own interests, his energy and enthusiasms were maintained throughout his life and were all directed toward the attainment of his goal.

By way of introduction Doctor Fulton quotes from Ferris Greenslet (Walter Pater, 1903) a reference to the task of the biographer: "He will undertake to deal fairly with his reader, to be diligent in gathering knowledge of his subject, to order it carefully, to ponder it strictly and sympathetically; but he will not undertake to portray the elusive personality in all its fulness." The biographer has taken this to heart. It is difficult to see how the many facets of Doctor Cushing's make-up could have been portrayed with justice or accuracy by any author. All of them were not presented to any one person. Likewise, they were not all visible in any one phase of his career. The reviewer has been impressed with the sustained interest the book has held. Doctor Fulton deserves praise for a task well done, and the subject of the biography would, I am sure, be gratified with the

GYNECOLOGICAL AND OBSTETRICAL PATHOLOGY. By Emil Novak, A.B., M.D., D.Sc. (Hon. Dublin), F.A.C.S. Second edition, with 542 illustrations, 15 in color. W. B. Saunders Company, Philadelphia, 1947. Price \$7.50.

Anyone who treats gynecologic disturbances and performs gynecological operations should be fully conversant with the underlying pathology of the disease. As medical studies go, formal training in gynecologic pathology is skimpy. The average doctor promptly forgets the little that he was taught during his student days. Evidently Emil Novak realized this when he wrote the original edition of his book, because it brought knowledge in simple language to those wishing to enhance their store of pathological information. The book was then well received by specialists and general practitioners alike. The second edition, just off the press, has been enriched by a large number of illustrations, some of them in color, and by an occasional change in the text. Novak's first edition was so complete in its scope that little could be added to the subject matter without endangering the scope of the book. As the new edition stands, it preserves its highly practical and simple character. It is thoroughly scientific in its approach, but handles the subject matter so skillfully that it is an easy book to read. It is well indexed and although it does not pretend to be an encyclopedia, it is an excellent reference book. Subjects such as endometrial disturbances, carcinoma of the uterus and ovary, have been brought up to date. The discussion of the dysontogenetic tumors of the ovary is classically concise and complete. It should be read by every doctor or student. Hellman, who contributed the chapter on placental abnormalities, likewise has revised and enlarged his contribution. The Saunders Company have done an excellent job of printing and binding and of reproducing good illustrations well.

You may not have the time nor the inclination to pick up your gynecological pathology where you left off during your student days. Nor may you find the time to slave away at the microscope to learn the intricacies of pathological diagnosis, but you can find time to read Novak's enlightening book. It will give you an insight into the subject which will make it easy for you to evaluate your pathologist's reports, not to speak of the better understanding it will give you of the disturbances you treat or operate upon. All in all, Novak's book, if read intelligently, is like taking a postgraduate course in gynecologic pathology in a comfortable chair by your fireside.

\*\*:TRODUCTION TO SURGERY. By Virginia Kneeland Frantz, M.D., Assistant Professor of Surgery, College of Physicians and Surgeons, Columbia University; Associate Attending Surgical Pathologist, Presbyterian Hospital, New York, and Harold Dortic Harvey, M.D., Assistant Professor of Clinical Surgery, College of Physicians and Surgeons, Columbia University; Assisting Attending Surgeon, Presbyterian Hospital, New York. Copyright 1946. Oxford University Press, New York. Price \$2.50.

This new book presents the most refreshing approach to the understanding of the principles of surgery that the reviewer has seen. It has been written primarily to aid the medical student as he is introduced to the surgical branch of medicine. But its context will be of great benefit to teachers of surgery, to doctors who practice surgery and to all physicians who should have at least an acquaintance in surgery.

Simple, clear language and steadfast adherence to fact stimulate the reader's interest. Honesty and open-mindedness in evaluation of surgical treatment and theory encourage him to share the author's zeal to seek understanding. The purpose of the treatise, and the manner in which it is constructed can be realized from these quotations, taken from the introductory paragraphs. "We offer the student beginning the study of modern surgery certain fundamental observations on the response of the tissues of the body to various types of injury, and the repair that follows . . ." "Surgery is defined as that branch of medicine which attempts: 1. To assist the body to repair injuries. 2. To improve anatomical deformities and physiological derangements. 3. To assist the body in overcoming certain infections. 4. To remove or destroy certain neoplasms.'

Elsewhere in the inrtoduction, there is explanation for many of the problems that baffle the beginning student in surgery, such as the reason why surgical terminology sometimes is at variance with that of other branches of medicine. The authors stress the importance of observation and of clinical experience as the basis for each individual's concept of surgical disease and treatment. They offer the reminder that the surgeon also must be concerned with other branches of medicine, for surgical disease oftentimes exists concomittantly with "non-surgical" disease. After the general introduc-

tory remarks, the evolution and the present day knowledge of surgery is then unfolded in systematic

In a concise seven pages, the history of surgery is reviewed from 1550 B.C. through the Golden Age of Greece, the Dark Ages and the Renaissance to the three great surgeons of all time: Paré, John Hunter and Lister. The reader notices that surgery began with the study of infections and injuries which occurred in areas of the body that could be observed objectively. He may reflect that the knowledge of these same phenomena is just as fundamental in present day surgery. He may find it interesting that the repression of surgery by the Church in the Dark Ages became the origin for the practice of minor surgery by barbers.

After the historical review, the book is divided into eight sections which are arranged to fulfill the definition of surgery as indicated in paragraph two of this review. The authors are careful first to establish the truth or what is known of the truth, and, second, to present familiar examples of the process or disease under discussion with brief generalizations as to treatment. Among the latter are included chemotherapeutic and antibiotic agents whose proven actions are stated with particular honesty. The doubtful and "hoped-for" actions of these drugs are omitted.

The basic principles of surgery include the pathology of injury and inflammation and the physiology of repair of all types of tissues from these processes. The mechanism of infections of all kinds is reviewed, and the problem of surgical drainage is clarified. Separate sections are devoted to foreign bodies, wounds, ulcers, burns and gangrene. The final section is concerned with hemorrhage and shock, with the clinical aspects of a carefully taken history and of a properly performed physical examination, and with a word of stimulation to the reader for experimental surgery.

Efficiency of expression and not brevity is the premium for the entire monograph. The reader will feel great respect for the considerable labor by the authors which produced this introduction to surgery so completely, so clearly, so well-organized.

N.B. Typographical error, last line of last paragraph of page 107, apportunity instead of opportunity.

CUSHNY'S PHARMACOLOGY AND THERAPEUTICS. Thirteenth Edition, thoroughly revised by Arthur Grollman, A.B., Ph.D., M.D., F.A.C.P., and Donald Slaughter, B.S., M.D. Illustrated with 74 engravings. Lea & Febiger, Philadelphia. 1947. Price \$8.50.

This revision of a standard reference book in Pharmacology and Therapeutics is the most recent and best work of its kind which has appeared since the war. It will be an invaluable aid to the practicing physician and student alike, who desire to learn of recent advances in such agents as: curare and its modifications, histamine and anti-histamine compounds, folic acid, the antimalarials—chloroquine and paludrine, dimercaprol (B.A.L.) as an antidote against arsenic, radio-active phosphorus, the barbiturates including pentothal, the local anesthetics including metycaine, the sulfonamides in-

cluding sulfomylon and promin, the antibodies including streptomycin and tyrothricin, and many other new drugs developed during the war period.

The outstanding section is on the hormones, it might be read by all interested in the use of endocrine preparations. Except for the small space devoted to mode of action, this section is unique among currently available textbooks. The section on the anterior pituitary is complete and up-to-date and avoids the complex factors involved in the various gonadotrophins. The section on the posterior pituitary is also timely. The section on the thyroid gland is complete except for reference to the role that the thyroid plays in promoting absorption. Thiouracil is briefly discussed with the intimation that it has definite drawbacks in chronic use. The section on the adrenal cortex reflects the interest of the senior author.

Unfortunately the section on toxicology does not include reference to the considerable number of economic poisons that are becoming problems in clinical practice.

THE DIAGNOSIS AND TREATMENT OF BRON-CHIAL ASTHMA. By Leslie N. Gay, M.D., Ph.B., Assistant Professor of Medicine of the Johns Hopkins University School of Medicine, Director of the Allergy Clinic of the Johns Hopkins Hospital. With a forward by Warfield T. Longcope, A.B., M.D., Professor of Medicine of the Johns Hopkins University School of Medicine. Physician-in-Chief of the Johns Hopkins Hospital. Copyright 1946. The Williams & Wilkins Company, Baltimore. Price \$5.00.

This book is an excellent presentation of the subject of bronchial asthma, its diagnosis and treatment. It actually is a monograph on the subject because it does not deal with the other allergic syndrome. It is recommended to the general practitioner and specialist but it is too limited in its scope for the medical student. The arrangement of the text is excellent and is written with great clarity and in a readable manner. Dr. Gay uses case histories to demonstrate the many and sundry problems in treating bronchial asthma.

The chapter on physiology of normal respiration and the asthmatic state, written in simple and understandable language, covers the subject very thoroughly. The section on pathology is a review of the literature on the subject plus the author's own observations which covers the subject quite thoroughly.

Twenty of the 35 pages devoted to etiology are given to a discussion of pollens and their relation to bronchial asthma (which includes charts of pollen and spore counts). Very little consideration is given to the problem in regions other than the Atlantic Coast. Much of the space could have been devoted to other pollen problems of other areas. The illustrations are excellent and of practical value.

Much space is devoted to a discussion of therapy in treatment of bronchial asthma; a great deal of which is useless, having been discarded and of questionable value. It would have been better if the author had given this space to his own experience

and routine procedures in the treatment of bronchial asthma.

Very little mention is made of the new antihistamine drugs and practically no discussion as to their value.

The allergy specialist will find much in this volume with which he will disagree, but there is a great deal of useful information. In conclusion one can say that here is another book on the subject.

PRINCIPLES OF HEMATOLOGY. By Russell L. Haden, M.A., M.D. Third Edition, thoroughly revised, published 1946. Octavo, 366 pages, with 171 illustrations including 173 original photomicrographs and 95 original charts and drawings. Cloth, \$5.00. Lea & Febiger, Washington Square, Philadelphia 6, Pa.

This is the third edition of a book on hematology written by a physician whose name has long been associated with diseases arising from disturbed hematopoesis. Since Dr. Haden has contributed much to the techniques of hemoglobin estimation and the various blood indices, it would be anticipated that the section on techniques in this book would be outstanding. Such is the case, and the methods are so clearly described that it makes this book of value to students and physicians alike. The book is of practical value to the physician in that it is illustrated by 106 pertinent clinical abstracts illustrating various types of hematopoetic disorders. In addition, the newer knowledge concerning the etiology of various types of anemia is made readily understandable by simple graphic illustrations. As a background for a clinical interpretation of various blood disorders. Dr. Haden has emphasized the technique of aspiration of marrow and interpretation of film preparations.

It was with regret that this reviewer did not find some mention of the RH Factor since the author had done so much on the hemolytic anemias. The book in general will be found of value to student and physician alike.

THE NATIONAL FORMULARY, Eighth Edition. Prepared by the Commission on National Formulary under the Supervision of the Council by authority of the American Pharmaceutical Association. Official from April 1, 1947. Published by the American Pharmaceutical Association. Washington 7. D. C. 1946, Price \$7.50.

In text arrangement, this eighth edition of the National Formulary, which on April 1, 1947, is officially to supersede the seventh edition, makes a notable departure from that used heretofore. Although monographs still are arranged in alphabetical sequence, in the new edition a monograph on a basic drug is followed by monographs on its official preparation. A marginal index is used to make the new arrangement easier to use. Another feature is that greater emphasis is put on the use of the metric system, although equivalents in the apothecaries system also are given.

Purpose of the new, as of preceding editions, is the establishment and promulgation of official standards for drugs.